ORGANIC SYNTHESES

I

ACETONE CYANOHYDRIN

$$(CH_3)_2CO + NaCN + H_2SO_4 \rightarrow (CH_3)_2C(OH)CN + NaHSO_4$$

Submitted by R. F. B. Cox and R. T. Stormont.
Checked by Reynold C. Fuson and Madison Hunt.

1. Procedure

In a 5-l. three-necked, round-bottomed flask fitted with an efficient stirrer (Note 1), a separatory funnel, and a thermometer in a well, is placed a solution of 500 g. (9.7 moles) of powdered 95 per cent sodium cyanide in 1200 cc. of water and 900 cc. (713 g., 12.3 moles) of acetone. The flask is surrounded by an ice bath and the solution is stirred vigorously. When the temperature falls to 15°, 2100 cc. (8.5 moles) of 40 per cent sulfuric acid (Note 2) is added over a period of three hours, keeping the temperature between 10° and 20°. After all the acid has been added the stirring is continued for fifteen minutes and then the flask is set aside for the salt to settle. Usually a layer of acetone cyanohydrin forms and is decanted and separated from the aqueous layer. The sodium bisulfate is removed by filtration and washed with three 50-cc. portions of acetone. The combined filtrate and acetone washings is added to the aqueous solution which is then extracted three times with 250-cc. portions of ether (Note 3). The extracts are combined with the cyanohydrin previously separated and dried with anhydrous sodium sulfate. The ether and acetone are removed by distillation from a water bath, and the residue is distilled under reduced pressure. The low-boiling portion is discarded and the acetone cyanohydrin is collected at 78–82°/15 mm. The yield is 640–650 g. (77–78 per cent of the theoretical amount).

2. Notes

1. It is advantageous to use a heavy metal stirrer because of the increased viscosity of the mixture toward the end of the reaction. Since some hydrogen cyanide tends to escape from the reaction mixture, the stopper carrying the stirrer should be fitted with a tube for leading off the gas or the reaction should be carried out under a hood.

2. The 40 per cent sulfuric acid is prepared by adding 650 cc. of concentrated sulfuric acid (sp. gr. 1.84) to 1800 cc. of water.

3. Extraction and distillation should be started as soon as possible after the completion of the reaction, and the distillation should be done as rapidly as possible to avoid decomposition.

3. Methods of Preparation

Acetone cyanohydrin has been prepared from acetone and anhydrous hydrogen cyanide in the presence of a basic catalyst such as potassium carbonate, potassium hydroxide, or potassium cyanide;[1] by the reaction of potassium cyanide on the sodium bisulfite addition product of acetone;[2] and by the action of hydrogen cyanide, prepared directly in the reaction mixture, on an aqueous solution of acetone.[3]

[1] Urech, Ann. **164**, 256 (1872); Ultée, Ber. **39**, 1857 (1906); Rec. trav. chim. **28**, 7 (1909).

[2] Bucherer and Grolée, Ber. **39**, 1225 (1906); Ger. pat. 141,509 [Chem. Zentr. **74**, I, 1244 (1903)].

[3] Welch and Clemo, J. Chem. Soc. **1928**, 2629.

II

DIAZOMETHANE

$$CH_3N(NO)CONH_2 + KOH \rightarrow CH_2N_2 + KCNO + 2H_2O$$

Submitted by F. Arndt.
Checked by C. R. Noller and I. Bergsteinsson.

1. Procedure

In a 500-cc. round-bottomed flask are placed 60 cc. of 50 per cent aqueous potassium hydroxide solution and 200 cc. of ether. The mixture is cooled to 5°, and 20.6 g. (0.2 mole) of nitrosomethyl urea (p. 48) is added with shaking. The flask is fitted with a condenser set for distillation, the lower end of which carries an adapter passing through a two-holed rubber stopper and dipping below the surface of 40 cc. of ether contained in a 300-cc. Erlenmeyer flask and cooled in an ice-salt mixture. The exit gases are passed through a second 40-cc. portion of ether likewise cooled below 0°. The reaction flask is placed in a water bath at 50° and brought to the boiling point of the ether with occasional shaking. The ether is distilled until it comes over colorless, which is usually the case after two-thirds of the ether has been distilled (Note 1). The combined solutions in the receivers contain from 5.3 to 5.9 g. of diazomethane (63–70 per cent of the theoretical amount) (Notes 2 and 3), which is sufficiently dry for most purposes. If a dry solution is required, it is allowed to stand for three hours over pellets of pure potassium hydroxide (Note 4). For extremely dry solutions, further drying may be carried out with sodium wire (Notes 5, 6, and 7).

2. Notes

1. In no event should all the ether be distilled.

2. For analysis an aliquot portion (about one-twentieth) of the solution is allowed to react at 0° with a solution of an accu-

rately weighed sample of about 1.3 g. of pure benzoic acid in 50 cc. of absolute ether. The benzoic acid must be in excess as evidenced by the complete decolorization of the diazomethane solution. The unreacted benzoic acid is titrated with standard 0.2 *N* alkali.

3. The same procedure may be used for preparing two or three times the quantity obtained here.

4. Broken sticks should not be used as the sharp corners facilitate the decomposition of the diazomethane.

5. The ether solution does not contain ammonia or methyl alcohol. It does contain traces of methylamine, but this is also the case when prepared from nitrosomethylurethan.

6. Diazomethane is an especially insidious poison. A person may work with it carelessly for some time without noticeable effects. This leads, however, to a super-sensitivity so that it is almost impossible to work even carefully with diazomethane without being subjected to attacks of asthma or fever.

7. If one does not require a pure, water-free solution, as is frequently the case when carrying out tests with small amounts of material, a simplified procedure may be used. To 100 cc. of ether is added 30 cc. of 40 per cent potassium hydroxide, and the mixture is cooled to 5°. To this with continued cooling and shaking is added 10 g. of finely powdered nitrosomethylurea in small portions over a period of one to two minutes. The deep yellow ether layer can be decanted readily; it contains about 2.8 g. of diazomethane, together with some dissolved impurities and water. The latter may be removed by drying for three hours over pellets of pure potassium hydroxide. Solutions of diazomethane in benzene and other water-immiscible organic solvents may be prepared in the same way.

3. Methods of Preparation

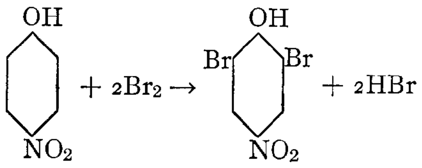
The procedure given here is essentially that which has recently appeared in the literature.[1] The only other methods of preparative importance are the action of alcoholic potassium hydroxide[2] or sodium dissolved in glycol[3] on nitrosomethylurethan,

and heating a mixture of potassium hydroxide, chloroform, and hydrazine hydrate.[4]

[1] Arndt and co-workers, Z. angew. Chem. **43**, 444 (1930); **46**, 47 (1933).
[2] v. Pechmann, Ber. **27**, 1888 (1894); **28**, 855 (1895).
[3] Meerwein and Burneleit, ibid. **61**, 1845 (1928).
[4] Staudinger and Kupfer, ibid. **45**, 505 (1912).

III

2,6-DIBROMO-4-NITROPHENOL



Submitted by W. W. Hartman and J. B. Dickey.
Checked by L. F. Fieser and C. H. Fisher.

1. Procedure

In a 5-l. round-bottomed flask fitted with a liquid-sealed mechanical stirrer, a dropping funnel, and a tube leading to a gas trap (Org. Syn. **14**, 2) to carry off the hydrogen bromide, 278 g. (2 moles) of *p*-nitrophenol (m.p. 112–113°) is dissolved in 830 cc. of glacial acetic acid. To this solution at room temperature is added dropwise with stirring during the course of three hours a solution of 750 g. (240 cc., 4.7 moles) of bromine in 700 cc. of glacial acetic acid. After the addition of the bromine the reaction mixture is stirred for one-half hour and then warmed on the steam bath (internal temperature about 85°) for one hour in order to remove as much of the excess bromine as possible. The last traces of bromine are removed by passing a stream of air into the reaction mixture, which then has a yellow or brown color. The mixture is treated with 1100 cc. of cold water, stirred until cool (Note 1), and allowed to stand in ice, or in an ice chest, overnight. The pale yellow crystalline product is collected on a 19-cm. Büchner funnel and washed first with 500 cc. of 50 per cent aqueous acetic acid and then thoroughly with water. It is dried in an oven at 40–60° or in a vacuum desiccator over sodium hydroxide. The yield is 570–583 g. (96–98 per cent of

the theoretical amount) of a nearly colorless product melting with decomposition at 138–140° (Note 2).

2. Notes

1. If the solution is stirred during cooling the product does not tend to cake on the walls of the flask and the resulting crystals are easier to wash.

2. This material is sufficiently pure for most purposes, and the quality is not greatly improved by recrystallization from 50 per cent acetic acid. Samples prepared by bromination, even after purification, invariably decompose at the melting temperature, which is somewhat dependent upon the rate of heating. The material obtained by nitration has been found to melt without decomposition at 144–145°.[1]

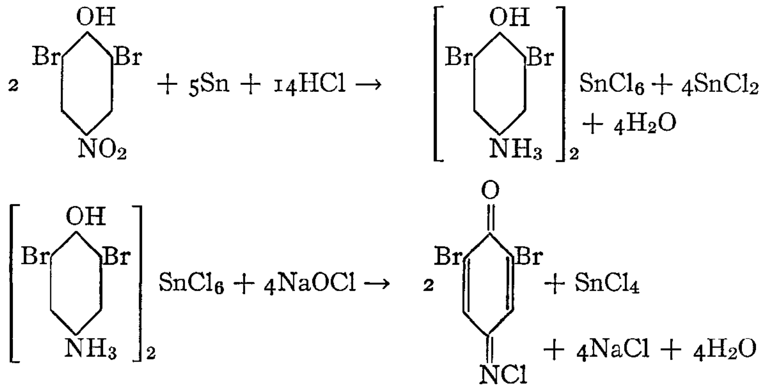
3. Methods of Preparation

2,6-Dibromo-4-nitrophenol has been prepared by the nitration of 2,6-dibromophenol [1] or of dibromophenol sulfonic acid,[2] and by the action of nitric acid on 2,6-dibromo-4-nitroso-phenol [3] or on 2,4,6-tribromophenol.[4] It has been obtained from the corresponding ethyl ether [5] and by the action of bromine on *p*-nitrosophenol,[6] 4,6-dibromo-2-nitrophenol,[7] 5-nitro-2-hydroxybenzoic acid,[8] and 5-nitro-2-hydroxybenzenesulfonic acid.[9] The dibromination of *p*-nitrophenol [10,13] has been carried out in sulfuric acid solution [11] and in the presence of aluminum chloride.[12] The method described here is essentially that of M¨hlau and Uhlmann.[13]

[1] Pope and Wood, J. Chem. Soc. **101**, 1828 (1912).
[2] Armstrong and Brown, ibid. **25**, 859 (1872).
[3] Kehrmann, Ber. **21**, 3318 (1888); Forster and Robertson, J. Chem. Soc. **79**, 688 (1901).
[4] Raiford and Heyl, Am. Chem. J. **43**, 395 (1910).
[5] Jackson and Fiske, Ber. **35**, 1132 (1902); Am. Chem. J. **30**, 60 (1903).
[6] van Erp, Rec. trav. chim. **30**, 290 (1911).
[7] Armstrong, J. Chem. Soc. **28**, 522 (1875); Ling, ibid. **51**, 147 (1887).
[8] Lellmann and Grothmann, Ber. **17**, 2731 (1884).
[9] Post, Ann. **205**, 94 (1880).
[10] Brunck, Z. Chem. **1867**, 204; ibid. **1868**, 323; Vaubel, J. prakt. Chem. [2] **49**, 544 (1894).
[11] Datta and Bhoumik, J. Am. Chem. Soc. **43**, 310 (1921).
[12] Bodroux, Compt. rend. **126**, 1285 (1898); Bull. soc. chim. [3] **19**, 759 (1898).
[13] Möhlau and Uhlmann, Ann. **289**, 94 (1896).

IV

2,6-DIBROMOQUINONE-4-CHLOROIMIDE



Submitted by W. W. HARTMAN, J. B. DICKEY, and J. G. STAMPFLI.
Checked by L. F. FIESER and C. H. FISHER.

1. Procedure

(*A*) 2,6-*Dibromo-4-aminophenol Chlorostannate.*—In a 5-l. round-bottomed flask is placed 148.5 g. (0.5 mole) of 2,6-dibromo-4-nitrophenol (p. 6) with 300 cc. (3.6 moles) of concentrated hydrochloric acid (sp. gr. 1.19), 300 cc. of water, and 185 g. (1.56 gram atoms) of mossy tin. Three cubic centimeters of capryl alcohol is added to control the foaming, and the mixture is heated in the open flask with stirring on the steam bath until the reaction starts. The reaction may proceed vigorously at the outset, and it is well to heat cautiously during the initial stages. Hydrochloric acid and water are added from time to time, and foaming can be controlled by the addition of a part of the water. A total of 520 cc. (6.2 moles) of concentrated hydrochloric acid and 900 cc. of water are added during the course of the reaction.

When the first, vigorous reaction is over the mixture is heated strongly until the dibromonitrophenol has all dissolved, and the hot solution (at about 85°) is filtered through a layer of decolorizing carbon (Norite) on a hot Büchner funnel. The filtrate, which usually is colorless, is cooled to 0° with stirring for two hours, or allowed to stand in a cool place overnight. The product, which separates in the form of colorless or slightly yellow needles, is collected on a Büchner funnel and washed with cold dilute hydrochloric acid (one volume of concentrated acid to one volume of water). The material is usually colorless and may be used directly for the reaction which follows (Note 1). After drying in an oven at 50–60°, or in a vacuum desiccator over sodium hydroxide, the tin salt weighs 214–220 g. The theoretical weight, based on the formula assumed above, is 217 g.

(*B*) 2,6-*Dibromoquinone-4-chloroimide.*—The chlorostannate is conveniently oxidized in two batches (Note 2). In a 3-l. flask is placed a solution of 115 g. (2.9 moles) of sodium hydroxide in 175 cc. of water, 1 kg. of cracked ice is added, and 108 g. (1.52 moles) of chlorine gas is passed into the mixture. About 80 per cent of the ice is melted by the operation. In a 5-l. flask 110 g. (0.56 mole) of the tin salt of 2,6-dibromo-4-aminophenol is dissolved in 1200 cc. of water and 12 cc. of concentrated hydrochloric acid. Solution is effected by warming the mixture to 40–50°, after which it is cooled to 15–17° and 600 g. of ice is added. The sodium hypochlorite solution is then added all at once with vigorous stirring (hood). A yellow precipitate of 2,6-dibromoquinone-4-chloroimide separates immediately and chlorine is evolved. As soon as the sodium hypochlorite solution has been stirred in, 120 cc. of concentrated hydrochloric acid is added in order to keep the tin salts in solution (Note 3). The fine, yellow precipitate is filtered under the hood on a Büchner funnel (Note 4) and washed with 1.5 l. of 5 per cent hydrochloric acid to remove tin salts and chlorine. The product is dried on a glass tray at 30–40° (Note 5), or in a vacuum desiccator over sodium hydroxide. From two such batches the yield of chloroimide melting at 80–82° is 126–130 g. (84–87 per cent of

the theoretical amount based on the weight of 2,6-dibromo-4-nitrophenol used in Part A).

2. Notes

1. If the product has an appreciable yellow color, it should be recrystallized from a mixture of 150 cc. of concentrated hydrochloric acid and 375 cc. of water, heating to 85–90°. The yield of recrystallized product is 180–190 g. By evaporating the mother liquor to one-third the original volume under reduced pressure, an additional 15–25 g. of tin salt can be recovered.

2. As much as 700 g. of tin salt can be oxidized in one run by using a 70-l. crock for the reaction vessel.

3. The particle size of the chloroimide can be increased by stirring for one hour at this point.

4. The first liter of filtrate is refiltered until it is clear.

5. Care must be taken in drying as one larger run decomposed violently in an open tray when the temperature was about 60°.

3. Methods of Preparation

2,6-Dibromoquinone-4-chloroimide has been prepared by the action of sodium hypochlorite on 2,6-dibromo-4-aminophenol in the form of the chlorostannate [1] or as the hydrochloride.[2]

[1] Möhlau, Ber. **16**, 2845 (1883); Friedländer and Stange, ibid. **26**, 2262 (1893); Möhlau and Uhlmann, Ann. **289**, 94 (1896).

[2] Gibbs, J. Biol. Chem. **72**, 653 (1927).

V

DI-*n*-BUTYLCARBINOL

$$C_4H_9Br + Mg \rightarrow C_4H_9MgBr$$

$$2C_4H_9MgBr + HCO_2C_2H_5 \rightarrow (C_4H_9)_2CHOMgBr + C_2H_5OMgBr$$

$$2(C_4H_9)_2CHOMgBr + H_2SO_4 \rightarrow 2(C_4H_9)_2CHOH + MgBr_2 + MgSO_4$$

Submitted by G. H. Coleman and David Craig.
Checked by John R. Johnson and H. B. Stevenson.

1. Procedure

In a 3-l. three-necked, round-bottomed flask fitted with a 500-cc. separatory funnel, a liquid-sealed mechanical stirrer, and a reflux condenser, are placed 36.5 g. (1.5 gram atoms) of magnesium turnings and 500 cc. of absolute ether. A solution of 206 g. (1.5 moles) of *n*-butyl bromide (Org. Syn. Coll. Vol. 1, 26) in 250 cc. of absolute ether is placed in the separatory funnel. The stirrer is started and 10–15 cc. of the bromide solution is allowed to flow into the flask from the funnel; the reaction generally begins within a few minutes (Note 1). As soon as refluxing is vigorous, the flask is surrounded by ice and water and the rate of addition of the bromide is adjusted so that moderate refluxing occurs. After all the solution has been added (thirty to forty minutes), the cooling bath is removed. Stirring is continued for fifteen minutes longer, after which only a small residue of unreacted magnesium remains.

The flask is cooled in an ice bath and a solution of 55.5 g. (0.75 mole) of pure ethyl formate (Note 2) in 100 cc. of absolute ether is placed in the separatory funnel. The stirrer is started and the ethyl formate solution is added at such a rate that the ether refluxes gently. This addition requires about one-half

hour. The cooling bath is then removed and the stirring is continued for ten minutes.

While stirring vigorously (Note 3), 100 cc. of water is added through the separatory funnel at such a rate that rapid refluxing occurs. Following this, a cold solution of 85 g. (46 cc., 0.85 mole) of concentrated sulfuric acid in 400 cc. of water is added. After the addition of the acid, the two layers become practically clear. A large part of the ethereal layer is decanted into a 1-l. round-bottomed flask, and the remainder, together with the aqueous layer, is transferred to a separatory funnel. The solid remaining in the flask is washed with two 25-cc. portions of ether, which are added to the material in the separatory funnel. The ethereal layer is separated and combined with the decanted portion. The flask is fitted with an efficient fractionating column, and the ether is distilled from a steam bath until the temperature of the vapor reaches about 50°. To the residual impure carbinol (Note 4) is added 75 cc. of 15 per cent aqueous potassium hydroxide solution and the flask is fitted with a reflux condenser. The mixture is boiled vigorously under reflux for three hours, after which the purified carbinol is removed by steam-distillation, keeping the volume in the flask at 250–300 cc. The distillate is collected in a separatory funnel, so that the lower aqueous layer can be drawn off periodically. The distillation is complete when about 1500 cc. of water has been collected.

The upper layer of di-*n*-butylcarbinol is separated and allowed to stand over 10 g. of anhydrous potassium carbonate for one hour. The liquid is decanted into a 500-cc. Claisen flask, and the residual potassium carbonate is washed with three 10-cc. portions of dry ether, which are added to the material in the distilling flask. After removing a small fraction of low-boiling material, there is obtained 90–92 g. (83–85 per cent of the theoretical amount) of pure di-*n*-butylcarbinol, b.p. 97–98°/20 mm. (Note 5).

2. Notes

1. The reaction between the ethereal solution of *n*-butyl bromide and the magnesium generally starts without any

assistance; if necessary, a small amount of a previously prepared Grignard reagent or a crystal of iodine may be used to start the reaction.

2. It is best to use freshly distilled ethyl formate, which may be purified in the following way: To 100 g. of commercial ethyl formate is added 15 g. of anhydrous potassium carbonate, and the mixture is allowed to stand for one hour with occasional shaking. The ester is decanted into a dry 200-cc. flask, and 5 g. of phosphorus pentoxide is added. The flask is provided with an efficient fractionating column, and the ethyl formate is distilled into a receiver protected from atmospheric moisture. A fraction boiling at 53–54° was used in this preparation.

3. During the addition of the water it is necessary to stir efficiently so that the solid which is produced will be precipitated in a finely divided form and not in large aggregates.

4. The formic ester of di-*n*-butylcarbinol is present as an impurity in the crude product and is hydrolyzed by refluxing with potassium hydroxide solution.

5. Di-*n*-butylcarbinol can be distilled at atmospheric pressure without appreciable decomposition (b.p. 193–194°/743 mm.) but it is preferable to distil under diminished pressure. The following boiling points were observed under various pressures: 97°/20 mm., 104°/30 mm., 109°/40 mm., 117°/60 mm., 130°/100 mm.

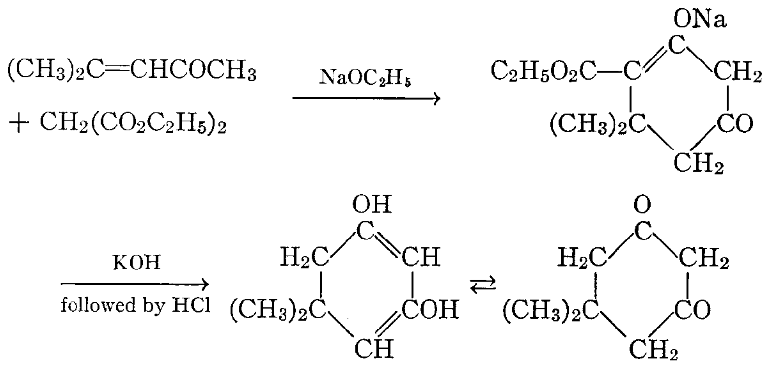
3. Methods of Preparation

Di-*n*-butylcarbinol has been prepared by the action of *n*-butylmagnesium bromide upon *n*-valeraldehyde[1] and upon ethyl formate.[1,2] It has also been obtained by the catalytic hydrogenation of di-*n*-butyl ketone in the presence of platinum.[3]

[1] Malengreau, Bull. acad. roy. Belg. cl. sci. **1906**, 802 [C.A. **1**, 1970 (1907)].
[2] Dillon and Lucas, J. Am. Chem. Soc. **50**, 1713 (1928).
[3] Vavon and Ivanoff, Compt. rend. **177**, 453 (1923).

VI

5,5-DIMETHYL-1,3-CYCLOHEXANEDIONE
(5,5-Dimethyldihydroresorcinol; Methone; Dimedone)



Submitted by R. L. SHRINER and H. R. TODD.
Checked by W. H. CAROTHERS and W. L. MCEWEN.

1. Procedure

IN a dry 2-l. three-necked, round-bottomed flask fitted with a liquid-sealed stirrer, a 500-cc. dropping funnel, and an efficient reflux condenser protected at the top with a calcium chloride tube, is placed 400 cc. of absolute alcohol. Through the condenser tube is added 23 g. (1 gram atom) of clean sodium at such a rate that the solution is kept at the boiling temperature. After the sodium has dissolved completely, 170 g. (1.06 moles) of diethyl malonate is added and then 100 g. (1.02 moles) of mesityl oxide (Note 1) is added slowly through the dropping funnel. The solution is refluxed with constant stirring for two hours, after which a solution of 125 g. (2.2 moles) of potassium hydroxide in 575 cc. of water is added and the mixture is stirred and refluxed again on the water bath for six hours.

The mixture while still hot is made just acid to litmus with dilute hydrochloric acid (1 volume concentrated acid to 2 volumes water; sp. gr. 1.055). About 550 cc. is required. The flask is fitted with a condenser set for distillation, and as much alcohol as possible (about 550 cc.) is distilled by heating on a water bath.

The residue in the flask is boiled with about 15 g. of decolorizing charcoal (Norite) (Note 2), filtered, and the treatment with charcoal repeated. It is again neutralized to litmus with dilute hydrochloric acid (about 150 cc.) and again boiled with charcoal. The hot, neutral or alkaline, yellow filtrate is finally made distinctly acid to methyl orange with additional dilute hydrochloric acid (50 to 100 cc.), boiled for a few minutes, and allowed to cool, whereupon the methone crystallizes. The product is filtered by suction from the acid liquid, washed with ice-cold water, and dried in the air. The yield is 96–122 g. (67–85 per cent of the theoretical amount) (Note 3).

2. Notes

1. The yield of methone depends on the purity of the mesityl oxide (Org. Syn. Coll., Vol. **1**, 338), which should be freshly distilled, collecting the fraction boiling at 126–131°.

2. Caution must be used in adding the decolorizing charcoal as the hot acid solution is likely to foam vigorously owing to the liberation of carbon dioxide. A large container should be used, and the charcoal should be added very slowly.

3. The submitters in carrying out this preparation invariably obtained yields ranging from 120 to 128 g. of a product melting between 145° and 147°. Crystallization from acetone (about 1 l.) gave 100 g. (70 per cent) of pure white material melting at 147°. The checkers (using mesityl oxide purchased from the Eastman Kodak Co. and freshly distilled) obtained yields ranging from 96 to 112 g. but their product melted at 147–148° and recrystallization failed to raise the melting point. The melting point of methone is given in the literature as 148–150°.

3. Methods of Preparation

5,5-Dimethyl-dihydroresorcinol has always been made from mesityl oxide and malonic ester. The procedure given above is that of Vorländer.[1]

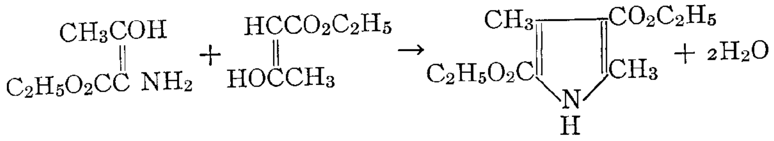
[1] Vorländer and Erig, Ann. **294**, 314 (1897); Vorländer, Z. anal. Chem., **77**, 245 (1929); Z. angew. Chem. **42**, 46 (1929); Chavanne, Miller, and Cornet, Bull. soc. chim. Belg. **40**, 673 (1931).

VII

2,4-DIMETHYL-3,5-DICARBETHOXYPYRROLE

$$CH_3COCH_2CO_2C_2H_5 + HNO_2 \rightarrow CH_3COCH(NO)CO_2C_2H_5 + H_2O$$

$$CH_3COCH(NO)CO_2C_2H_5 + 4[H](Zn + HOAc) \rightarrow CH_3COCH(NH_2)CO_2C_2H_5 + H_2O$$



Submitted by Hans Fischer.
Checked by C. R. Noller.

1. Procedure

In a 3-l. three-necked, round-bottomed flask fitted with a liquid-sealed mechanical stirrer and dropping funnel are placed 390 g. (379 cc., 3 moles) of ethyl acetoacetate (Org. Syn. Coll. Vol. 1, 230) and 900 cc. of glacial acetic acid. The solution is cooled in an efficient freezing mixture to 5°, and a cold solution of 107 g. (1.47 moles) of 95 per cent sodium nitrite in 150 cc. of water is added dropwise with vigorous stirring at such a rate that the temperature remains between 5° and 7°. With efficient cooling about one-half hour is required to add the nitrite, and the mixture is stirred for one-half hour longer. It is then allowed to stand for four hours during which time it warms up to room temperature.

The separatory funnel is replaced by a wide-bore condenser and the third neck of the flask is fitted with a stopper. The solution is stirred and portions of 196 g. (3 gram atoms) of zinc

dust (Note 1) are added quickly through the third neck of the flask until the liquid boils and then frequently enough to keep it boiling (Note 2). After the addition has been completed, the mixture is heated by a burner and refluxed for one hour (Note 3). The hot contents are decanted from the remaining zinc into a crock containing 10 l. of water which is being vigorously stirred. The zinc residue is washed with two 50-cc. portions of hot glacial acetic acid which are also decanted into the water. After standing overnight, the crude product is filtered by suction, washed on the filter with two 500-cc. portions of water, and dried in air to constant weight. The yield is 205–230 g. (57–64 per cent of the theoretical amount) melting at 126–130°. On recrystallizing a 50-g. portion from 100 cc. of 95 per cent alcohol and washing twice with 20-cc. portions of cold alcohol, there is obtained 38.5 g. of pale yellow crystals melting at 136–137° (Note 4).

2. Notes

1. The zinc dust should be at least 80 per cent pure and an amount used equivalent to 196 g. of 100 per cent material. An excess of zinc dust up to 3.5 gram atoms has been used without changing the yield.

2. Four portions of approximately 15 g. each are required to bring the solution to the boiling point after which the remainder is added in about 5-g. portions over a period of three-quarters of an hour. Great care must be taken not to add too much zinc dust at first as the mixture foams badly. It is well to have a bath of ice and water and wet towels handy in order to control the reaction if it should become too violent.

3. For reasons unknown some runs behave entirely differently from others. Occasionally the foaming suddenly stops after about half of the zinc has been added and the remainder can be added much more rapidly, causing the solution to boil vigorously. During the period of external heating of the solution the mixture becomes thick and gummy and as much as 300 cc. of acetic acid must be added before stirring can be continued. The lower yields reported are obtained when this occurs.

4. The crude product turns pink when exposed to light whereas the recrystallized product is quite stable. A somewhat lighter product is obtained if 2 g. of decolorizing carbon is used during the crystallization, but this has no effect on the melting point.

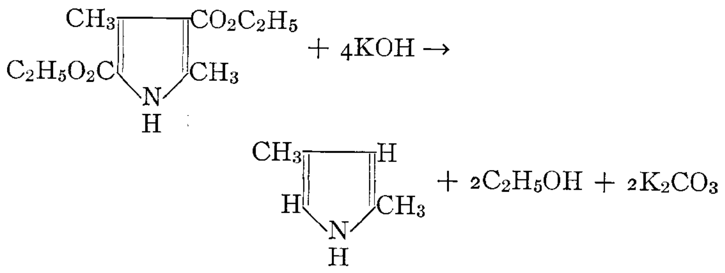
3. Methods of Preparation

The above procedure, which has always been used for the preparation of 2,4-dimethyl-3,5-dicarbethoxypyrrole, is essentially that of Knorr.[1]

[1] Knorr, Ann. **236**, 318 (1886).

VIII

2,4-DIMETHYLPYRROLE



Submitted by Hans Fischer.
Checked by C. R. Noller.

1. Procedure

A solution of 270 g. (4.8 moles) of potassium hydroxide in 150 cc. of water is prepared in a 3-l. round-bottomed flask, 120 g. (0.5 mole) of crude 2,4-dimethyl-3,5-dicarbethoxypyrrole (p. 17) and a pinch of sand are added, and the whole is mixed thoroughly by shaking. The flask is fitted with a reflux condenser, and the mixture is heated in an oil bath at 130° for two to three hours with occasional shaking until the thick paste has become partially liquefied owing to the formation of dimethylpyrrole.

The flask is next fitted for distillation with superheated steam and with a separatory funnel for the introduction of water into the center of the flask. A 3-l. round-bottomed flask fitted with a vertical condenser is used as a receiver, being connected directly to the inclined condenser from the distillation flask (Org. Syn. Coll. Vol. 1, 467, Fig. 24). The temperature of the oil bath is raised to 160° and superheated steam at 220–250° is introduced. The temperature of the oil bath is then gradually raised to 200°.

If foaming becomes too great, a few drops of water are added from the separatory funnel, being careful that the water does not strike the hot glass walls (Note 1). Steam distillation is continued until no more dimethylpyrrole comes over. This takes from one to two hours, and the distillate amounts to 2.5–3 l. The distillate is extracted once with 200 cc. of ether and three times with 100-cc. portions and the extract dried for two hours over 20 g. of anhydrous potassium carbonate. The ether is removed by distillation from a 100-cc. modified Claisen flask having a 15-cm. fractionating side arm (Org. Syn. Coll. Vol. 1, 125), the solution being added gradually through a separatory funnel. After the ether is removed the residue is distilled and the fraction boiling at 160–165° is collected. The yield is 27 to 30 g. (57–63 per cent of the theoretical amount) (Notes 2 and 3).

2. Notes

1. If the contents of the flask cake or become semi-solid, the temperature of the oil bath should be lowered and the rate of flow of superheated steam gradually decreased.

2. There is practically no fore-run, but if repeated or larger batches are made it is possible to obtain about 2 g. more of product per run from the higher-boiling fractions. If recrystallized ester is used a higher yield of dimethylpyrrole with less high-boiling products is obtained but the over-all yield is lower.

3. 2,4-Dimethylpyrrole is very readily oxidized in the air to a red resinous substance. If it is not used immediately, it should be stored under nitrogen or sealed in a glass vial under a vacuum.

3. Methods of Preparation

2,4-Dimethylpyrrole has been obtained by a large number of reactions, but the method of Knorr,[1] of which the above procedure is a modification, and the condensation of acetone with aminoacetone[2] are the only ones of preparative interest.

[1] Knorr, Ann. **236**, 326 (1886).
[2] Piloty and Hirsch, ibid. **395**, 65 (1913).

IX

2,4-DINITROANILINE

$$(NO_2)_2C_6H_3Cl + 2NH_3 \rightarrow (NO_2)_2C_6H_3NH_2 + NH_4Cl$$

Submitted by F. B. WELLS and C. F. H. ALLEN.
Checked by REYNOLD C. FUSON and CHAN MANN LU.

1. Procedure

A WIDE-MOUTHED 250-cc. flask (Note 1) containing a mixture of 50 g. (0.25 mole) of technical 2,4-dinitrochlorobenzene (Note 2) and 18 g. (0.23 mole) of ammonium acetate is half immersed in an oil bath. The flask is fitted with a reflux condenser and an inlet tube, the lower end of which is at least 2 cm. wide (to prevent clogging), and nearly touches the surface of the reaction mixture. During the operation ammonia gas is introduced through a bubble counter which contains a small amount of strong potassium hydroxide solution (12 g. of potassium hydroxide in 10 cc. of water).

The oil bath is heated to 170° and maintained at that temperature for six hours during which time ammonia gas is passed through at the rate of three to four bubbles per second. After the mixture has cooled, the solid is broken up by means of a glass rod, mixed with 100 cc. of water, and the mixture heated to boiling and filtered while hot. The residue is dissolved in 500 cc. of boiling alcohol, and water is added (about 150 cc.) until the solution becomes turbid. Heat is applied until the turbidity disappears and then the solution is allowed to cool. After standing overnight, the crystals are filtered and dried. The yield is 31–35 g. (68–76 per cent of the theoretical amount) of 2,4-dinitroaniline, melting at 175–177° (Notes 3 and 4). For further purification it is recrystallized in the above manner from alcohol and water, using 20 cc. of alcohol per gram of solid. Ninety per cent

of the crude material is recovered as recrystallized product melting sharply at 180°.

2. Notes

1. The neck of the flask must be large enough to admit the wide inlet tube. A 250-cc. extraction flask is most convenient.

2. The technical dinitrochlorobenzene used had a freezing point of 45°. The higher yield given is obtained using a product once recrystallized from alcohol (m.p. 48°).

3. Some specimens of technical dinitrochlorobenzene used contained undetermined impurities that formed double compounds with the dinitroaniline. These remained in the filtrate. It was not worth the trouble to recover the small amount of amine thus lost.

4. The value of this method is that it obviates the necessity of using an autoclave. It was not satisfactory when applied to the nitrochlorobenzenes.

3. Methods of Preparation

2,4-Dinitroaniline has been prepared by heating dinitrochlorobenzene and ammonia under pressure;[1] by heating 1,2,4-trinitrobenzene with concentrated ammonia;[2] by heating dinitrochlorobenzene with urea[3] or ammonium acetate;[4] by hydrolysis of the dinitroacetanilide obtained when dinitrochlorobenzene and acetamide are heated at 200–210°;[5] by heating 2,4-dinitroanisole or 2,4-dinitroanisic acid with aqueous or alcoholic ammonia under pressure;[6] by heating 2,4-dinitrophenol and aqueous ammonia under pressure;[7] and by the rearrangement of *p*-nitrophenylnitroamine spontaneously[8] or with concentrated sulfuric acid at 0°.[9]

[1] Clemm, J. prakt. Chem. [2] **1**, 170 (1870); Willgerodt, Ber. **9**, 979 (1876).
[2] Hepp, Ann. **215**, 362 (1882).
[3] Pfister, U. S. pat. 1,752,998 [C. A. **24**, 2468 (1930)].
[4] Brit. pat. 169,688 [C. A. **16**, 721 (1922)].
[5] Kym, Ber. **32**, 3539 (1899).
[6] Salkowski, Ann. **174**, 263 (1874).
[7] Barr, Ber. **21**, 1542 (1888).
[8] Bamberger and Dietrich, ibid. **30**, 1253 (1897).
[9] Hoff, Ann. **311**, 98 (1900).

X

n-DODECYL BROMIDE

(Lauryl Bromide)

$$C_{12}H_{25}OH + HBr \rightarrow C_{12}H_{25}Br + H_2O$$

Submitted by E. Emmet Reid, John R. Ruhoff, and Robert E. Burnett.
Checked by W. H. Carothers and W. L. McEwen.

1. Procedure

In a 500-cc. distilling flask fitted with a thermometer and an inlet tube leading to the bottom (Note 1), is placed 186 g. (1 mole) of *n*-dodecyl alcohol (Note 2). An adapter, one end of which is immersed in about 75 cc. of water contained in a 125-cc. Erlenmeyer flask, is attached to the side arm of the flask. All connections are of rubber. The alcohol is heated to 100°, and dry hydrogen bromide (Note 3) is passed in at 100–120° (Note 4) until no more absorption occurs (Note 5). The crude bromide, together with any of the product that has been carried over into the receiving flask, is transferred to a separatory funnel, separated from the aqueous hydrobromic acid formed during the reaction, and shaken with one-third its volume of concentrated sulfuric acid (Note 6). The lower acid layer is drawn off and discarded (Note 7). The residual bromide is mixed with an equal volume of 50 per cent methyl alcohol (Note 8), and aqueous ammonia is added with intermittent shaking until the solution is alkaline to phenolphthalein. The lower bromide layer is drawn off and washed once with an equal volume of 50 per cent methyl alcohol. It is then dried with calcium chloride, filtered, and distilled. The yield of product boiling at 199.5–201.5°/100 mm. or 134–135°/6 mm. is 220 g. (88 per cent of the theoretical amount) (Note 9).

2. Notes

1. In order to obtain more efficient absorption of the hydrogen bromide, a small bulb is blown on the end of the inlet tube, and a number of pin holes are made in it by means of a small, white-hot tungsten wire.
2. The dodecyl alcohol used was obtained by the fractionation of "Lorol"; its boiling point was 192.5–193.5°/100 mm. or 151–152°/21 mm. If the alcohol is not of good quality, the yield is somewhat lower. It may also be prepared according to the procedure given in Org. Syn. **10**, 62.
3. The hydrogen bromide is conveniently prepared by the direct combination of hydrogen and bromine (p. 35). An excess of hydrogen is to be avoided since it causes loss of product by volatilization.
4. The heat of the reaction maintains the alcohol at this temperature until the preparation is nearly completed.
5. For each mole of alcohol about 1.5 moles of hydrogen bromide is required, of which 1 mole is used to convert the alcohol to the bromide and approximately 0.5 mole to saturate the water formed in the reaction. The rate of addition should be regulated so as to require not less than an hour and a half. The Erlenmeyer flask that serves as a receiver should be weighed with the water in it before it is put in place. When the reaction is complete, the receiver gains weight rapidly, and becomes warm owing to the heat of solution of the hydrogen bromide in the water.
6. The crude bromide must be shaken well with the sulfuric acid. The function of the sulfuric acid appears to be to convert any free alcohol to the acid sulfate, which is then soluble in 50 per cent methyl alcohol and ammonia.
7. Care must be taken that the separation of the two layers in this and subsequent washings is complete. Failure to observe this precaution is usually the cause of a low yield.
8. The use of methyl alcohol prevents, to a large extent, the formation of troublesome emulsions. Less than 0.1 g. of dodecyl bromide dissolves in 100 cc. of 50 per cent methyl alcohol at room temperature.

9. The authors have prepared other bromides by this method with the yields indicated below:

Bromide	*Yield, %*	*Solubility of bromides in methyl alcohol*
Cyclohexyl	72–75	Less than 1 g. in 100 cc. of 65% methyl alcohol
n-Heptyl	87–90	Less than 0.5 g. in 100 cc. of 50% methyl alcohol
Tetradecyl	88–89	Less than 0.1 g. in 100 cc. of 50% methyl alcohol
Octadecyl	90–91	Practically insoluble in 90% methyl alcohol

Obviously for the lower bromides it is desirable to use no more methyl alcohol than is necessary to prevent the formation of an emulsion. A convenient method is to place the water, phenolphthalein, and crude bromide in a separatory funnel, and add ammonia until the mixture becomes pink. Methyl alcohol is then added in small portions until the emulsion is broken and two layers separate with a distinct boundary after the mixture has been agitated.

3. Methods of Preparation

The above method for preparing *n*-dodecyl bromide is an adaptation of that of Ruzicka[1] and has been published recently.[2] It is thought to present some advantages in ease of manipulation and quality of product over the older method involving the action of aqueous hydrobromic acid on the alcohol in the presence of sulfuric acid.[3]

[1] Ruzicka, Stoll, and Schinz, Helv. Chim. Acta, **11**, 685 (1928).
[2] Ruhoff, Burnett, and Reid, J. Am. Chem. Soc. **56**, 2784 (1934).
[3] Kamm and Marvel, J. Am. Chem. Soc. **42**, 299 (1920); Org. Syn. Coll., Vol. **1**, 27.

XI

n-HEXADECANE

$$C_{16}H_{33}I + 2[H](Zn + HCl) \rightarrow C_{16}H_{34} + HI$$

Submitted by P. A. Levene.
Checked by W. W. Hartman, L. A. Smith, and J. B. Dickey.

1. Procedure

In a 2-l. round-bottomed flask fitted with a liquid-sealed mechanical stirrer, a gas inlet tube, and a tube to carry off hydrogen chloride and acetic acid vapors (Note 1), are placed 915 cc. of glacial acetic acid, 327 g. (5 gram atoms) of zinc dust, and 352 g. (1 mole) of cetyl iodide (m.p. 20–22°) (p. 29). The mixture is saturated with dry hydrogen chloride (Org. Syn. Coll. Vol. **1**, 520) and then stirred and heated on a steam bath. At the end of every five hours of heating, the mixture is again saturated with hydrogen chloride. After the reaction has proceeded for twenty-five hours, the mixture is allowed to cool, and the layer of hexadecane, which rises to the top of the reaction mixture, is separated. The residue is poured into 3 l. of water and filtered on a Büchner funnel to remove the zinc dust. The zinc dust is washed with 500 cc. of water and then with 250 cc. of ether. The combined water layers are extracted with two 500-cc. portions of ether. The ether extracts are combined, added to the hexadecane, and the resulting solution is washed with two 250-cc. portions of 20 per cent sodium hydroxide, and then with water until free of alkali. The ether solution is dried with 150 g. of anhydrous sodium sulfate, filtered, and distilled from a 500-cc. modified Claisen flask with a fractionating side arm. The yield of *n*-hexadecane boiling at 156–158°/14 mm. and melting at 16–17° is 192 g. (85 per cent of the theoretical amount).

2. Notes

1. If the reaction is carried out under a hood, an open flask may be used.

3. Methods of Preparation

n-Hexadecane has been prepared by treating octyl iodide with sodium,[1] by distilling mercury dicetyl with zinc dust or by heating mercury dicetyl in a closed tube at 200°,[2] by heating palmitic acid with hydroiodic acid and red phosphorus,[3] and by treating cetyl iodide with red phosphorus and hydroiodic acid, or with zinc and hydrochloric acid in alcohol[4] or in acetic acid solution.[5] It has been obtained as a by-product from the preparation of octylmagnesium bromide[6] and from the action of sodium on a mixture of octyl bromide and ethyl bromide,[7] and is one of the products formed on heating sodium stearate[8] or cetyl ether.[9]

[1] Zincke, Ann. **152**, 1 (1869).
[2] Eichler, Ber. **12**, 1882 (1879).
[3] Krafft, ibid. **15**, 1701 (1882).
[4] Sorabji, J. Chem. Soc. **47**, 38 (1885).
[5] Levene, West and van der Scheer, J. Biol. Chem. **20**, 523 (1915).
[6] v. Braun, Deutsch and Schmatloch, Ber. **45**, 1254 (1912).
[7] Lachowicz, Ann. **220**, 180 (1883).
[8] Grün and Wirth, Ber. **53**, 1310 (1920).
[9] Oddo, Gazz. chim. ital. **31**, I, 346 (1901) [Chem. Zentr. **72**, II, 180 (1901)].

XII

n-HEXADECYL IODIDE

(Cetyl Iodide)

$$3C_{16}H_{33}OH + PI_3 \rightarrow 3C_{16}H_{33}I + H_3PO_3$$

Submitted by W. W. Hartman, J. R. Byers, and J. B. Dickey.
Checked by W. H. Carothers and W. L. McEwen.

1. Procedure

Two hundred and forty-two grams (1 mole) of cetyl alcohol (Org. Syn. **10**, 64) (m.p. 48–49°) (Note 1), 10 g. (0.32 gram atom) of red phosphorus, and 134 g. (1.06 gram atoms) of resublimed iodine are placed in a 3-l. round-bottomed flask and heated in an oil bath until the alcohol has melted. The flask is then fitted with a reflux condenser and a liquid-sealed mechanical stirrer. With stirring, the mixture is heated at 145–150° (temperature of the oil bath) for five hours. When the reaction mixture has cooled, the cetyl iodide is removed by extracting once with a 250-cc. portion and twice with 125-cc. portions of commercial ether. The combined ether extracts are filtered free of phosphorus and washed with 500 cc. of cold water, 250 cc. of 5 per cent sodium hydroxide solution, and again with 500 cc. of water. The ether solution is dried over anhydrous calcium chloride. After removal of the ether by distilling on a steam bath, the iodide is distilled under reduced pressure. The main fraction, distilling at 220–225°/22 mm. (210–215°/12 mm.), weighs 300 g. (85 per cent of the theoretical amount) and melts at 18–20° (Note 2). Redistillation gives 275 g. (78 per cent of the theoretical amount) boiling at 220–223°/22 mm. (203–205°/9 mm.) and melting at 20–22° (Note 3).

2. Notes

1. When a poorer grade of cetyl alcohol is used, the yield may be reduced to as low as 70 per cent.

2. This material is probably pure enough for most work. Melting points as high as 25° are recorded in the literature.

3. Traces of iodine come over when the distillation starts and the fore-run is therefore strongly colored. When distillation is started again after being interrupted traces of iodine again appear in the first few drops of the main distillate. A more nearly colorless distillate is obtained if means are provided for cutting fractions without interrupting the distillations.

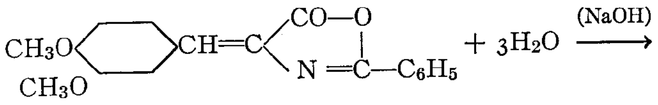
3. Methods of Preparation

The method described is essentially that of Smith.[1] Several other workers have used a similar method.[2] Cetyl iodide has also been prepared by heating cetyl alcohol with yellow phosphorus and iodine in carbon disulfide solution,[3] and by repeatedly passing dry hydrogen iodide acid into the molten alcohol and permitting the reaction mass to stand between additions.[4]

[1] Smith, J. Chem. Soc. **1932**, 738.
[2] Fridau, Ann. **83**, 9 (1852); Levene, West, and van der Scheer, J. Biol. Chem. **20**, 521 (1915); Delcourt, Bull. soc. chim. Belg. **40**, 284 (1931) [C. A. **25**, 5661 (1931)].
[3] Gascard, Ann. chim. [9] **15**, 372 (1921).
[4] Krafft, Ber. **19**, 2219 (1886).

XIII

HOMOVERATRIC ACID
(3,4-Dimethoxyphenylacetic Acid)



$$(CH_3O)_2C_6H_3CH_2COCO_2H + NH_3 + C_6H_5CO_2H$$

$$(CH_3O)_2C_6H_3CH_2COCO_2H + H_2O_2 \xrightarrow{(NaOH)} (CH_3O)_2C_6H_3CH_2CO_2H + H_2O + CO_2$$

Submitted by H. R. Snyder, J. S. Buck, and W. S. Ide.
Checked by John R. Johnson and P. W. Vittum.

1. Procedure

(*A*) *Methyl Homoveratrate.*—In a 3-l. round-bottomed flask are placed 1 l. of 10 per cent sodium hydroxide solution and 200 g. (0.65 mole) of the azlactone of α-benzoylamino-β-(3,4-dimethoxyphenyl) acrylic acid (m.p. 149–150°) (Org. Syn. **13**, 8). The flask is fitted with a reflux condenser and immersed in an oil bath so that the inner level is lower than the oil level of the bath (Note 1). The mixture is refluxed gently for six to seven hours, until the evolution of ammonia is complete. The resulting solution contains the sodium salts of 3,4-dimethoxyphenylpyruvic acid (Note 2) and benzoic acid.

To the above aqueous solution contained in a 2-l. wide-mouthed Erlenmeyer flask, is added 85 cc. of 40 per cent sodium hydroxide solution. The flask is equipped with a mechanical stirrer and is cooled in an ice-salt mixture. With stirring, 75 cc. of 30 per cent hydrogen peroxide (Merck's "Superoxol")

diluted with 75 cc. of water is added at such a rate that the temperature does not rise above 15°. After standing for about ten hours at room temperature (preferably overnight) the solution is acidified by the cautious addition (Note 3) of 450 cc. of concentrated hydrochloric acid (sp. gr. 1.19). The warm acid solution is extracted with one 400-cc. portion and two 200-cc. portions of warm benzene. The combined benzene extracts are dried over anhydrous magnesium sulfate and filtered through a cotton plug into a 3-l. round-bottomed flask.

The benzene is removed by distillation, 1 l. of methyl alcohol (Note 4) containing 15 cc. of concentrated sulfuric acid is added, and the flask is fitted with an efficient reflux condenser provided with a drying tube. After refluxing gently for five hours the condenser is set downward for distillation and the methyl alcohol is distilled from a steam bath. The residual liquid is cooled and shaken with 500 cc. of cold water. The mixture is transferred to a separatory funnel and extracted with one 400-cc. portion and two 200-cc. portions of benzene. The combined extracts are washed twice with 100-cc. portions of 10 per cent sodium carbonate solution and finally with two 100-cc. portions of water. After drying the benzene solution over anhydrous magnesium sulfate, it is transferred to a 2-l. flask and the benzene is distilled, using a steam bath. The residual mixture of methyl benzoate and methyl homoveratrate is transferred to a 250-cc. Claisen flask and distilled under reduced pressure. The first fraction, collected up to 100° at 16 mm., is methyl benzoate (b.p. 87°/16 mm.) and weighs about 75 g. (85 per cent of the theoretical amount. After a small intermediate fraction of 2–3 g., pure methyl homoveratrate is collected at 176–178°/16 mm. or 129–131°/1 mm. The yield is 76–82 g. (56–60 per cent of the theoretical amount, based on the azlactone).

(*B*) *Homoveratric Acid.*—In a 500-cc. round-bottomed flask are placed 250 cc. of 10 per cent sodium hydroxide solution and 76 g. (0.36 mole) of methyl homoveratrate. The flask is fitted with a reflux condenser and the mixture is boiled gently. The saponification proceeds rapidly and the ester layer disappears after about ten minutes. The mixture is refluxed gently for twenty minutes longer, after which the solution is cooled in an ice bath and then poured slowly, with stirring, into a mixture of 125 cc. of concentrated hydrochloric acid and 350 g. of ice. Crystals of the hydrate of homoveratric acid separate at once. After standing for about thirty minutes the crystalline product is filtered with suction and washed on the filter with two 25-cc. portions of ice water. The crystals are pressed thoroughly on the filter, pulverized, and allowed to stand overnight in a vacuum desiccator containing soda lime (to remove residual hydrochloric acid) and calcium chloride. The yield in the saponification is almost quantitative and amounts to 70 g. (55 per cent of the theoretical amount, based on the original azlactone). This product melts at 96–97° and contains traces of sodium chloride. For purification the acid is dissolved in 350 cc. of hot benzene and the solution is filtered. To the hot filtrate is added 150 cc. of hot ligroin (b.p. 70–80°), and the solution is covered with a watch glass and allowed to cool slowly. After standing for several hours (preferably overnight) in a cool place, the crystals are filtered with suction and washed with a cold solution of 35 cc. of benzene and 15 cc. of ligroin, followed by 50 cc. of cold petroleum ether. The solvent is removed as completely as possible by pressing on the filter and finally by allowing the product to stand in a vacuum desiccator (Note 5). The purified homoveratric acid weighs 65 g. (51 per cent of the theoretical amount, based on the original azlactone) and melts sharply at 98°.

2. Notes

1. The inner level is kept below that of the oil in order to avoid the otherwise uncontrollable bumping of the solution.

2. 3,4-Dimethoxyphenylpyruvic acid can be isolated from this solution in the following way (J. S. Buck and W. S. Ide). The aqueous solution of the sodium salts is saturated with sulfur dioxide, while the temperature is maintained below 40°. The benzoic acid precipitates and is filtered off with suction and washed with a small quantity of water. The filtrate and washings are placed in a 3-l. round-bottomed flask provided with a mechanical stirrer and heated to boiling. Concentrated hydro-

chloric acid is added cautiously, with stirring, until present in excess. The acid must be added carefully since there is a tendency for the solution to become supersaturated with sulfur dioxide, which is subsequently liberated with violence. A heavy precipitate of 3,4-dimethoxyphenylpyruvic acid separates, and after the reaction mixture has cooled, this is filtered with suction. After drying, the acid is washed with two 50-cc. portions of ether. The yield of 3,4-dimethoxyphenylpyruvic acid is 110–116 g. (76–80 per cent of the theoretical amount) and the product melts at 181–184°. It can be purified by crystallization from glacial acetic acid.

An alternative procedure for the preparation of homoveratric acid (J. S. Buck and W. S. Ide) consists in isolating the pyruvic acid and subjecting it to the oxidation process given in the second paragraph of part A. This variation obviates the esterification process but in the hands of the checkers did not prove as satisfactory as the one described.

3. Large quantities of carbon dioxide are evolved during the addition of the acid.

4. It is unnecessary to use especially dried methyl alcohol. High-grade commercial methanol is quite satisfactory.

5. Since the acid forms a hydrate it is advisable to minimize the exposure of the acid to atmospheric moisture.

3. Methods of Preparation

Homoveratric acid has been prepared by the methylation of homoprotocatechuic acid[1] and of homovanillic acid[2] with methyl iodide, and from veratric aldehyde through the azlactone and 3,4-dimethoxyphenylpyruvic acid.[3] The procedure given here is adapted from that last mentioned and from that used for the preparation of *p*-methoxyphenylacetic acid.[4]

[1] Pictet and Gams, Ber. **42**, 2949 (1909).
[2] Tiemann and Matsmoto, ibid. **11**, 143 (1878).
[3] Haworth, Perkin, and Rankin, J. Chem. Soc. **125**, 1693 (1924).
[4] Cain, Simonsen, and Smith, ibid. **103**, 1036 (1913).

XIV

HYDROGEN BROMIDE (ANHYDROUS)

$$H_2 + Br_2 \rightarrow 2HBr$$

Submitted by John R. Ruhoff, Robert E. Burnett, and E. Emmet Reid.
Checked by W. H. Carothers and W. L. McEwen.

1. Procedure

(*A*) *Apparatus.*—A 125-cc. distilling flask (B, Fig. 1) (Note 1) is fitted with a two-holed rubber stopper bearing a 50-cc. dropping funnel (Note 2) and an inlet tube about 6 mm. in diameter, both of which reach to the bottom of the flask. The latter is supported in an 800-cc. beaker which serves as a water bath. The side arm of the flask is connected by means of a

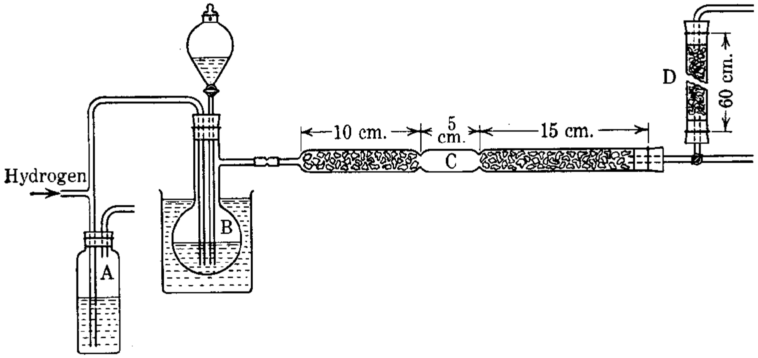


Fig. 1.

short piece of rubber tubing to the narrow end (Note 3) of the combustion tube C which is made of Pyrex glass and is 20 mm. in diameter (inside) and 30 cm. in length. It is packed with pieces of porous plate held in place by constrictions as shown in the figure, and it is supported at each end by a small clamp at a sufficient height to give a clearance of 3-4 cm. above a Bunsen burner. The open end of the tube is connected by means of

stoppers and a three-way stopcock (Note 4) to the vertical tube D, of the same diameter as C and 60 cm. long. This tube is packed with copper turnings to remove any uncombined bromine which may escape from the combustion tube. A safety bottle A containing water or some other suitable liquid and having a tube leading to the vent of the hood is placed in the train to provide an outlet for the hydrogen in case an obstruction is formed in the apparatus. It also provides a convenient method for determining the hydrogen pressure (Note 5). Hydrogen is obtained from a cylinder fitted with a reducing valve.

(*B*) *Operation.*—The tube D is disconnected from the combustion tube by turning the stopcock so that the gases pass directly to the hood. Bromine is placed in flask B; the water bath is heated to 38° and maintained at this temperature (Note 6). A slow stream of hydrogen is started through the apparatus, and when the combustion tube is completely filled with bromine vapors, a low flame is placed under the empty section of the combustion tube. Soon a small yellow flame appears inside the heated portion of the tube, and when all bromine vapor has been swept from the combustion tube, the latter is connected to the tube D (Note 7). The flame is adjusted to keep the lower part of the tube at a dull red heat; it may be necessary to raise or lower it, according to the rate of operation, and the hydrogen stream is regulated to give the desired output. The apparatus will conveniently produce 300 g. of hydrogen bromide per hour (Note 8).

2. Notes

1. It is convenient to bend the side arm of the distilling flask so that it is perpendicular to the neck.

2. The stopcock of the dropping funnel should be held in place by means of a rubber band.

3. The distilling flask may be connected to the combustion tube by means of a rubber stopper, but it is preferable to seal a piece of 6-mm. tubing to one end and to use a small piece of rubber tubing for the connection. Even with this arrangement the connection must be inspected from time to time to be sure

that the tube is not obstructed. It is still more satisfactory to use a ground glass joint.

4. The three-way stopcock may be dispensed with but it facilitates the starting operation and provides a quick method for venting the gas in case combination does not take place properly, thus preventing deterioration of the copper turnings.

5. When operating to produce about 300 g. of hydrogen bromide per hour the water level is depressed approximately 12 cm.

6. The vapor pressure of bromine should be maintained at half an atmosphere. The vapor pressure of bromine is reported as 324 mm. at 35° and 392 mm. at 40°. If the bath becomes too warm, it should be cooled at once with ice; otherwise more bromine will be evaporated than will combine with the hydrogen present.

A more convenient form of apparatus for the vaporization of bromine is shown in Fig. 2. This is the same in principle as that described in the above procedure, but the bromine container instead of being heated by warm water is heated by the vapor of boiling ethyl bromide (38.4°). Thus no attention to a water bath is required.

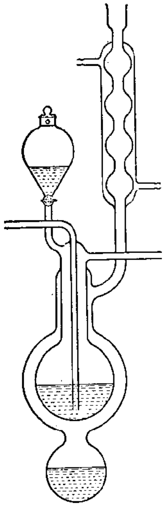


FIG. 2.

7. The copper turnings remove any trace of bromine that may be present by converting it to black cupric bromide. If the level of blackened copper rises, bromine is being carried over. The presence of a small quantity of moisture, however, will cause a slight darkening of all the copper.

If very dry hydrogen bromide is desired, a small trap surrounded by solid carbon dioxide and placed in the train will condense the water, and a small amount of hydrogen bromide. Care must be taken to prevent clogging of the trap.

8. According to the literature[1] the chief difficulties in the preparation of hydrogen bromide by combination of the elements are to avoid explosive combination on the one hand and spontaneous extinction of the flame on the other hand. Neither of these difficulties has been encountered in repeated opera-

tions extending over many hours with the apparatus described above.

3. Methods of Preparation

The very extensive literature on the preparation of hydrogen bromide is completely and concisely reviewed in Gmelin's "Handbuch."[1] The methods most commonly used involve the hydrolysis of certain bromides, particularly the action of bromine on red phosphorus and water; the action of bromine on hydrocarbons, particularly on tetralin; and the direct combination of the elements. The action of bromine on tetralin is a convenient one for small-scale laboratory operation.[2] The direct combination of the elements has certain advantages of simplicity and cleanliness, especially when considerable amounts of hydrogen bromide are required. Platinum and charcoal have frequently been used as catalysts but they can be dispensed with at sufficiently high temperatures.[3]

[1] Gmelin, "Handbuch der anorganischen Chemie," 8th ed., Part VII, p. 182, Verlag Chemie, Berlin, 1931.

[2] For details see Houben, "Die Methoden der organischen Chemie," 3rd ed., Vol. III, p. 1156, Verlag Georg Thieme, Leipzig, 1930.

[3] Ruhoff, Burnett, and Reid, J. Am. Chem. Soc. **56**, 2784 (1934).

XV

p-IODOPHENOL

$$2HOC_6H_4NH_2 + 3H_2SO_4 + 2NaNO_2 \rightarrow 2HOC_6H_4N_2SO_4H + Na_2SO_4 + 4H_2O$$

$$HOC_6H_4N_2SO_4H + KI \xrightarrow{(Cu)} HOC_6H_4I + N_2 + KHSO_4$$

Submitted by F. B. Dains and Floyd Eberly.
Checked by Reynold C. Fuson and H. H. Hully.

1. Procedure

One hundred and nine grams (1 mole) of *p*-aminophenol (Note 1) is dissolved in a mixture of 500 g. of ice, 500 cc. of water, and 65 cc. (120 g., 1.2 moles) of concentrated sulfuric acid (sp. gr. 1.84). To this solution, kept in a freezing mixture at 0°, is added during the course of an hour with constant mechanical stirring, a solution of 72 g. (1 mole) of 95 per cent sodium nitrite in 150 cc. of water. The stirring is continued twenty minutes longer, and then 20 cc. (37 g., 0.37 mole) of concentrated sulfuric acid is added.

This solution is poured into an ice-cold solution of 200 g. (1.2 moles) of potassium iodide in 200 cc. of water. After a few minutes, 1 g. of copper bronze (Note 2) is added, with continued stirring, and the solution is warmed slowly on the water bath. The temperature is kept at 75–80° until the evolution of nitrogen ceases; during this process the iodophenol separates as a heavy dark oil. After cooling to room temperature the reaction mixture is extracted three times with 165-cc. portions of chloroform and the combined extracts washed with dilute thiosulfate solution. The solvent is removed on the water bath and the residue distilled under reduced pressure, the *p*-iodophenol coming over

at 138–140°/5 mm. One crystallization from about 2 l. of ligroin (b.p. 90–110°) gives a colorless product melting sharply at 94°. The yield of recrystallized product is 153–159 g. (69–72 per cent of the theoretical amount).

2. Notes

1. The *p*-aminophenol used was a commercial product melting at 182–183° with decomposition.

2. Some commercial bronzes used for bronze paints are coated with a film of stearic acid. For chemical work an untreated pure copper bronze should be used.

3. Methods of Preparation

p-Iodophenol was first obtained as a by-product of the action of iodine on salicylic acid in alkaline solution or by heating iodosalicylic acid.[1] It has also been obtained by the action of iodine on phenol in alkaline solution[2] or in the presence of mercuric oxide,[3] or by the action of iodine monochloride.[4] It is best prepared by the diazotization of *p*-aminophenol and replacement of the diazonium group by iodine[5] although it has also been obtained from *p*-iodoaniline by diazotization and replacement of the diazonium group by hydroxyl.[6]

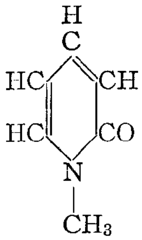
[1] Lautemann, Ann. **120**, 299 (1861); Kekulé, ibid. **131**, 221 (1864).
[2] Holleman and Rinkes, Rec. trav. chim. **30**, 96 (1911).
[3] Hlasiwetz and Weselsky, Ber. **2**, 523 (1869).
[4] Schützenberger and Sengenwald, Jahresber. **1862**, 413.
[5] Nölting and Wrzesinski, Ber. 8, 820 (1875); Nölting and Stricker, ibid. **20**, 3021 (1887); Neumann, Ann. **241**, 74 (1887).
[6] Griess, Zeit. für Chemie, **1865**, 427; Holleman and Rinkes, Rec. trav. chim. **30**, 95 (1911).

XVI

1-METHYL-2-PYRIDONE

$$C_5H_5N + (CH_3)_2SO_4 \rightarrow (C_5H_5NCH_3)SO_4CH_3$$

$$(C_5H_5NCH_3)SO_4CH_3 + 3NaOH + 2K_3Fe(CN)_6 \rightarrow$$



$$+ Na(CH_3)SO_4 + 2K_3NaFe(CN)_6 + 2H_2O$$

Submitted by E. A. Prill and S. M. McElvain.
Checked by C. S. Marvel and Sidney H. Babcock.

1. Procedure

In a 5-l. round-bottomed flask fitted with a separatory funnel and a reflux condenser, is placed 145 g. (1.83 moles) of dry pyridine (Note 1), and 231 g. (1.83 moles) of dimethyl sulfate is added dropwise through the separatory funnel. After the addition of the dimethyl sulfate the flask is heated in a boiling water bath for two hours to complete the reaction.

The flask containing the crude pyridinium salt is removed from the condenser and the salt dissolved in 400 cc. of water. The flask is fitted with a mechanical stirrer which will stir efficiently any volume of liquid which may be in the flask and the solution is cooled to 0° in an ice-salt bath. Separate solutions of 1200 g. (3.65 moles) of potassium ferricyanide in 2400 cc. of water and of 300 g. (7.5 moles) of sodium hydroxide in 500 cc. of water are prepared and added dropwise from two separatory funnels to the well-stirred solution of the pyridinium salt at such a rate that the temperature of the reaction mixture does not

rise above 10°. The rate of addition of these two solutions is regulated so that all the sodium hydroxide solution has been introduced into the reaction mixture when one-half of the potassium ferricyanide solution has been added. This usually requires about one hour. The second half of the potassium ferricyanide is then added over a period of about one hour. The reaction mixture is allowed to stand five hours during which time it comes to room temperature.

The 1-methyl-2-pyridone is salted out of the reaction mixture by the addition of 400–500 g. of anhydrous sodium carbonate to the well-stirred solution. When no more of the sodium carbonate dissolves, the stirring is discontinued and the yellow or brown oily layer containing most of the desired pyridone, together with some of the unreacted pyridinium salt, water, and inorganic salts, is separated from the aqueous mixture. The aqueous mixture is filtered (Note 2) to remove the excess sodium carbonate and the precipitated potassium or sodium ferrocyanide. The filtrate is divided into three portions, each of which is extracted twice with 200-cc. portions of technical iso-amyl alcohol (Note 3). The alcohol used for the second extraction of the first aqueous portion is satisfactory for the first extraction of a second aqueous portion, et cetera, so that a total volume of 800 cc. is used. The iso-amyl alcohol extracts are combined and added to the oily layer which was first separated from the reaction mixture. An aqueous layer usually appears and is separated and extracted with another 100-cc. portion of amyl alcohol.

The combined alcohol extract is distilled under reduced pressure from a modified Claisen flask (Org. Syn. Coll. Vol. 1, 125) by heating on a water bath. All the solvent is thus recovered for use in a subsequent preparation.

The residue is transferred to a 250-cc. modified Claisen flask and distilled under diminished pressure from an oil bath. There is almost no low-boiling fraction if the alcohol has been carefully removed. The yield of product boiling at 122–124°/11 mm. is 130–140 g. (65–70 per cent of the theoretical amount) (Notes 4 and 5). A small amount of black solid remains in the distillation flask after the pyridone has distilled.

2. Notes

1. A commercial medicinal grade of pyridine was used without further purification.

2. This operation is most satisfactory when a glass-wool plug placed in a glass funnel is used as the filter. The liquid in this funnel should be stirred to prevent the heavy precipitate from settling and clogging the filter.

3. The extraction of the pyridone from the aqueous solution is difficult when benzene or ether is used as a solvent. 1-Methyl-2-pyridone, when dry, is very soluble in ethyl ether, benzene, and most organic solvents. It is, however, practically insoluble in petroleum ether or ligroin. When a mixture of water, benzene, and a little pyridone is shaken together all the pyridone is found in the water layer. When the pyridone is salted out from water by adding a sufficient quantity of potassium carbonate, the oily layer does not dissolve when benzene or ethyl ether is added, but three layers are formed. The pyridone seems to be extracted by ether or benzene only when the aqueous solution is strongly saturated with sodium hydroxide or potassium hydroxide and then the tendency to form an emulsion is so great that separation of the layers is extremely difficult.

When equal volumes of water, technical iso-amyl alcohol, and a little pyridone are shaken together, the pyridone is found to be about equally distributed between the two solvents. Chloroform is also satisfactory for the extraction of pyridone from water.

4. The 1-methyl-2-pyridone when pure is odorless and colorless. It tends to turn dark on standing unless it is kept in a sealed tube.

5. The boiling points at other pressures are given by Fisher and Chur[4] as 250°/740 mm., 130°/14.5 mm., 126°/12.5 mm., and 121°/10 mm.

3. Methods of Preparation

1-Methyl-2-pyridone has been prepared by the methylation of 2-pyridone,[1] by the oxidation of 1-methylpyridinium iodide[2]

and of 1-methylpyridinium methyl sulfate[3] with a ferricyanide, and by the electrolytic oxidation of 1-methylpyridinium methyl sulfate.[4]

[1] v. Pechmann and Baltzer, Ber. **24**, 3144 (1891).
[2] Decker, J. prakt. Chem. [2] **47**, 28 (1893).
[3] Decker and Kaufmann, ibid. [2] **84**, 435 (1911); Fargher and Furness, J. Chem. Soc. **107**, 690 (1915).
[4] Fisher and Neundlinger, Ber. **46**, 2544 (1913); Neundlinger and Chur, J. prakt. Chem. [2] **89**, 466 (1914); Fisher and Chur, ibid. [2] **93**, 363 (1916).

XVII

o-NITROPHENYLSULFUR CHLORIDE
(*o*-Nitrobenzenesulfenyl Chloride)

$$NO_2C_6H_4SSC_6H_4NO_2 + Cl_2 \rightarrow 2NO_2C_6H_4SCl$$

Submitted by MAX H. HUBACHER.
Checked by L. F. FIESER and D. J. POTTER.

1. Procedure

IN a 1-l. three-necked flask fitted with a thermometer, a reflux condenser, and an inlet tube extending to the bottom of the flask and drawn out to a small opening, are placed 600 cc. of dry carbon tetrachloride, 154 g. (0.5 mole) of di-*o*-nitrophenyl disulfide, m.p. 193–195° (Org. Syn. Coll. Vol. **1**, 215), and 0.25 g. of iodine. To the upper end of the condenser is attached a glass tube which dips below the surface of a little carbon tetrachloride contained in a test tube. A current of chlorine, dried with sulfuric acid, is passed into the reaction mixture, the temperature of which is maintained at 50–60°. The rate of flow of the chlorine (about 16–17 g. per hour) is regulated so that little or no gas escapes through the carbon tetrachloride trap. The yellow di-*o*-nitrophenyl disulfide gradually disappears, and after two to two and one-half hours a homogeneous, dark yellow solution is obtained (Note 1). The warm solution is filtered from a small amount of dark residue through a warm Büchner funnel, rinsing the flask and filter with 30 cc. of warm carbon tetrachloride. The yellow filtrate (Note 2) is cooled to 5° and the product allowed to crystallize. The cake of crystals is broken with a rod, collected on a Büchner funnel, and drained well. The product is dried rapidly (two hours) at 50° and bottled (Note 3). This material melts at 73–74.5° and weighs 126–135 g. (66–71 per cent of the theoretical amount). A further crop is obtained by removing the solvent from the

mother liquor by distillation from a water bath (Note 4), the dark, residual oil being poured into an evaporating dish. The last traces of carbon tetrachloride are removed by drying at 50°, during which process the oil crystallizes. This material melts at 67–72° and weighs 48–58 g. It is pure enough for most purposes (Note 5). The total yield is 183–184 g. (96–97 per cent of the theoretical amount) (Notes 6 and 7).

2. Notes

1. An excess of chlorine will do no harm.

2. For many purposes this filtered solution can be used without purification after distilling about 100 cc. of the solvent to remove the excess chlorine. The yield of material in solution is considered as 98 per cent of the theoretical amount.

3. The pure material melts at 74.5–75°. When in contact with moist air, *o*-nitrophenylsulfur chloride decomposes within a few days, giving off hydrogen chloride. Stored in a brown, glass-stoppered bottle and sealed well, the material can be kept for many months.

4. Since *o*-nitrophenylsulfur chloride decomposes spontaneously when heated to about 170°, it is advisable to use a water bath when removing the solvent.

5. This material may be crystallized from hot carbon tetrachloride (2 cc. per gram), cooling the filtered solution to 5°. The recovery of a product melting at 70–73° is 75 per cent of the crude material.

6. Practically the same method can be used for the preparation of *o*-nitro-*p*-chlorophenylsulfur chloride (m.p. 95–97°); the chlorination of the disulfide (m.p. 212–213°) in this case proceeds much more slowly. 2,4-Dinitrophenylsulfur chloride can be prepared by the chlorination of the corresponding disulfide in nitrobenzene suspension at 120–130°. As the chloride is of an explosive nature the solvent must be removed by distillation in vacuo at 130°. The crude material melts at 89–92°. After crystallization from carbon tetrachloride it melts at 94–95°.

7. The arylsulfur chlorides are used for the introduction of the Ar-S- group, their reactions being analogous to those of acid chlorides.

3. Methods of Preparation

o-Nitrophenylsulfur chloride has always been prepared by the chlorination of the disulfide.[1]

[1] Zincke, Ber. **44**, 770 (1911); Zincke and Farr, Ann. **391**, 63 (1912).

XVIII

NITROSOMETHYLUREA

$$CH_3NH_2 \cdot HCl + KCNO \rightarrow CH_3NHCONH_2 + KCl$$

$$CH_3NHCONH_2 + HNO_2 \rightarrow CH_3N(NO)CONH_2 + H_2O$$

Submitted by F. Arndt.
Checked by C. R. Noller and I. Bergsteinsson.

1. Procedure

(*A*) *From Methylamine Hydrochloride.*—In 600 cc. of warm water contained in a 1.5-l. round-bottomed flask are dissolved 100 g. (1.48 moles) of methylamine hydrochloride (Org. Syn. Coll. Vol. 1, 340) (Note 1) and 150 g. (1.85 moles) of c.p. granular potassium cyanate. The solution is boiled gently for ten minutes and then vigorously for five minutes. The hot solution is filtered and added to a solution of 100 g. (1.38 moles) of 95 per cent sodium nitrite in 200 cc. of water. The whole is cooled to $-5°$ and poured in small portions with good mechanical stirring into a mixture of 600 g. of ice and 100 g. of concentrated sulfuric acid contained in a 3-l. beaker. The beaker is surrounded by an ice-salt mixture and the methylurea solution added at such a rate that the temperature does not rise above 0°. The addition requires about forty-five minutes.

The nitrosomethylurea separates as a crystalline, foamy precipitate which is filtered at once with suction and well pressed on the filter. The crystals are stirred to a paste with cold water (about 30 cc.), sucked as dry as possible (Note 2), and dried in a vacuum desiccator to constant weight. The yield is 120–140 g. (84–98 per cent of the theoretical amount) (Note 3).

(*B*) *From Ammonia and Dimethyl Sulfate.*—Four hundred cubic centimeters (6 moles) of 28 per cent aqueous ammonia solution (sp. gr. 0.9) is placed in a 2-l. round-bottomed flask

and cooled externally with an ice-salt mixture to $-5°$. Three hundred grams (220 cc., 2.38 moles) of technical dimethyl sulfate (Note 4) is added dropwise from a separatory funnel, with good mechanical stirring, at such a rate that the temperature does not rise above 20°. About thirty-five minutes is required for the addition (Note 5). The mixture is next heated for two hours on the steam bath and then boiled vigorously for fifteen minutes. The hot solution is poured into a 3-l. round-bottomed flask containing 250 cc. of water and 150 g. (1.85 moles) of c.p. granular potassium cyanate, boiled for twenty minutes, and filtered. A solution of 120 g. (1.65 moles) of 95 per cent sodium nitrite in 200 cc. of water is added to the filtrate, the whole cooled below 0° and poured slowly into a well-stirred mixture of 600 g. of ice and 120 g. of concentrated sulfuric acid as described above. By continuing as in the above procedure 60 to 65 g. of pure nitrosomethylurea is obtained (35–38 per cent of the theoretical amount) (Note 3).

2. Notes

1. The methylamine hydrochloride used in checking was prepared by neutralizing a commercial 33 per cent aqueous solution of methylamine with concentrated hydrochloric acid, evaporating to dryness, and crystallizing once from 95 per cent ethyl alcohol.

2. A sample of the moist product should dissolve completely in boiling methyl alcohol. If an appreciable residue of salt remains, which is usually not the case, the washing process is repeated. Each successive washing decreases the yield somewhat.

3. The preparations obtained in this way can be kept a year or longer in a refrigerator. It should not be kept above 20° for more than a few hours. At temperatures in the neighborhood of 30° it may undergo a sudden decomposition without explosion but with the evolution of irritating fumes. It has been reported that the stability is increased by the addition of a few drops of acetic acid.

4. No appreciable decrease in volume should be found when the dimethyl sulfate is shaken with an equal volume of cold water.

5. The addition can be completed in about fifteen minutes if a metal can is used as a container instead of a beaker.

3. Methods of Preparation

The procedures given here are essentially those which have recently appeared in the literature.[1] Nitrosomethylurea has also been prepared by the action of sodium nitrite and sulfuric acid on either methylurea nitrate[2] or methylurea.[3]

[1] Arndt and co-workers, Z. angew. Chem. **43**, 444 (1930); **46**, 47 (1933).
[2] Brüning, Ber. **21**, 1809 (1888); Ann. **253**, 6 (1889).
[3] Werner, J. Chem. Soc. **115**, 1095 (1919).

XIX

OLEYL ALCOHOL

(9,10-Octadecenol-1)

$$C_{17}H_{33}CO_2C_4H_9 + 4Na + 3C_4H_9OH \rightarrow C_{17}H_{33}CH_2OH + 4C_4H_9ONa$$

Submitted by E. E. Reid, F. O. Cockerille, J. D. Meyer, W. M. Cox, Jr., and J. R. Ruhoff.
Checked by C. R. Noller and R. Bannerot.

1. Procedure

A 5-l. round-bottomed flask is fitted with a wide-bore Y adapter and two wide-bore reflux condensers. Three liters of anhydrous butyl alcohol (Note 1) and 507 g. (1.5 moles) of butyl oleate (Note 2) are placed in the flask, and then 180 g. (7.8 atoms) of clean sodium, cut in approximately 2.5-cm. cubes, is added in one lot and the flask connected to the condensers. The reaction is rather sluggish at first requiring about one-half hour to reach the boiling point of the butyl alcohol (Note 3) but then becomes quite vigorous. With two condensers no difficulty is encountered in taking care of the reflux, but if the reaction becomes too vigorous or excessive foaming occurs, wet towels should be placed on the flask until the reaction is again under control (Note 4). Toward the end of the reaction the flask is placed on a heated sand bath and gentle refluxing maintained until all the sodium has reacted. The heating is stopped temporarily, 160 cc. of water is added gradually through the condenser, and the solution is again refluxed gently for one hour (Note 5). At the end of this time the heating is stopped and 1200 cc. of water is added. The flask is well shaken and the mixture allowed to separate into two layers. The lower aqueous layer of sodium hydroxide is siphoned off and discarded (Notes 6 and 11).

About 200 g. of solid sodium chloride (Note 7) is added to the flask and the butyl alcohol is removed by steam distillation (Note 8). The alcohol layer is separated while still hot (Note 9), transferred to a 1-l. beaker, and heated on a hot plate with stirring until the temperature reaches about 160°. By this time all the water is removed and foaming has stopped (Note 10). The hot liquid is transferred to a 1-l. Claisen flask having a 25-cm. fractionating side arm and distilled at 3 mm. After a small fore-run of 5-10 g., the main fraction boils at 177–183°/3 mm. and amounts to 330–340 g. (82-84 per cent of the theoretical amount) (Note 11).

2. Notes

1. Commercial butyl alcohol is dried by distillation through a 1-m. column and the portion boiling at 117.5–118.5° is used. The ordinary commercial alcohol is usually sufficiently pure so that the bulk of the alcohol remaining in the flask after the temperature at the top of the column reaches 117° need not be distilled but may be used directly for the reduction.

2. The butyl oleate was prepared by the alcoholysis of 3 kg. of cold-pressed olive oil by refluxing with 7 l. of butyl alcohol and 150 g. of concentrated sulfuric acid for 20 hours. The mixture was washed three times with 2.5-l. portions of saturated sodium chloride solution. During the last washing methyl orange was added to the solution and enough sodium carbonate was added to neutralize any acid remaining. The excess butyl alcohol was distilled and the residue carefully fractionated from a 2-l. Claisen flask having a 25-cm. fractionating side arm. A total of 3075 g. of distilled esters was obtained, of which 2422 g. (about 70 per cent based on the olive oil used) distilled at 204–208°/3 mm. and had approximately the theoretical iodine number. This product contains a small amount of saturated esters but it is considerably purer than can be obtained from commercial oleic acid and is satisfactory for most purposes.

3. If one wishes to reduce this time, external heat may be applied until the boiling point is reached. In a run in which the butyl alcohol was heated to boiling before the addition of the sodium, the reaction began more vigorously but the yield was practically unchanged.

4. The reaction mixture should not be cooled below the boiling point of the butyl alcohol as a continuously vigorous reaction is essential for good yields.

5. This saponifies any unreacted ester.

6. The procedure up to this point requires about three and one-half hours and should be continuous.

7. The sodium chloride prevents the formation of an emulsion during the steam distillation.

8. The butyl alcohol is readily recovered and dried with very little loss.

9. The soap, and possibly a high-boiling by-product, causes even the liquid alcohols to set to a jelly on cooling.

10. This procedure largely eliminates the difficulty caused by foaming at the start of the vacuum distillation.

11. The procedure as given is generally applicable for the reduction of esters to alcohols in excellent yields. When preparing the solid normal saturated alcohols, the procedure may be modified, if desired, to permit the recovery of the acid from the unreduced ester. After the alkali is removed the alcohol layer is washed with two successive portions of 20 per cent salt solution which are discarded. Neither the strong alkali nor the salt solutions remove an appreciable amount of organic acid. A solution of 50 g. of calcium chloride in 150 cc. of water is added to the butyl alcohol solution, the mixture is steam-distilled until the butyl alcohol is removed, and the flask and contents are allowed to cool. A hole is made in the cake of solid alcohol and the water layer removed. Two liters of toluene is added and the flask warmed and shaken until the alcohol dissolves and only fine crystals of the calcium salt of the unreduced acid remain. The solution is cooled to 35° and filtered with suction. The calcium soap is removed from the filter, warmed with about 500 cc. of toluene, cooled, filtered, and washed with a little more toluene. The combined toluene solutions may be concentrated and the alcohol crystallized, or the toluene may be completely distilled and the residue vacuum distilled. The insoluble calcium

soap may be decomposed, re-esterified, and used in a subsequent reduction.

3. Other Methods of Preparation

Oleyl alcohol has been previously prepared only by the reduction of ethyl oleate with sodium and absolute ethyl alcohol.[1] By substituting butyl alcohol for ethyl alcohol, the procedure is less time-consuming and less dangerous to carry out, and gives better yields.

[1] Bouveault and Blanc, Bull. soc. chim. [3] **121**, 1210 (1904); cf. Org. Syn. **10**, 62.

XX

ORTHANILIC ACID

(Aniline-*o*-sulfonic Acid; *o*-Aminobenzenesulfonic Acid)

$$(NO_2C_6H_4S-)_2 + 4[O](HNO_3) + Cl_2 \rightarrow 2\ NO_2C_6H_4SO_2Cl$$

$$NO_2C_6H_4SO_2Cl + H_2O \rightarrow NO_2C_6H_4SO_3H + HCl$$

$$NO_2C_6H_4SO_3H + 6[H](Fe + CH_3CO_2H) \rightarrow NH_2C_6H_4SO_3H + 2H_2O$$

Submitted by E. WERTHEIM.
Checked by REYNOLD C. FUSON and R. S. SCHREIBER.

1. Procedure

(*A*) *o-Nitrobenzenesulfonyl Chloride*.—A 3-l. three-necked, round-bottomed flask is fitted with an efficient liquid-sealed stirrer, a reflux condenser, and an inlet tube for introducing chlorine well beneath the surface of the liquid. A glass outlet tube leads from the reflux condenser to the hood. In the flask are placed 200 g. (0.65 mole) of di-*o*-nitrophenyl disulfide (Org. Syn. Coll. Vol. 1, 215) 1 l. of concentrated hydrochloric acid (sp. gr. 1.18), and 200 cc. of concentrated nitric acid (sp. gr. 1.42). A stream of chlorine is passed into the mixture at the rate of about two bubbles per second, and the solution is warmed on a steam bath to 70°. In about thirty minutes the disulfide melts and the solution becomes orange-red in color. After the disulfide has melted, the heating and addition of chlorine are continued for one hour. The sulfonyl chloride is separated immediately from the supernatant liquid by decantation, washed with two 300-cc. portions of warm water (70°) and allowed to solidify. The water is drained from the solid mass as completely as possible.

The washed chloride is dissolved in 140 cc. of glacial acetic acid at 50–60°, and the solution is quickly filtered by suction.

The filtrate is chilled by immersing the flask in cold water and is vigorously stirred in order to cause the sulfonyl chloride to separate in fine crystals. The mixture is now triturated thoroughly with a liter of cold water which is then decanted into a large Büchner funnel. The process is repeated twice. Finally, a liter of cold water is added to the mixture, and then 10 cc. of concentrated ammonium hydroxide (sp. gr. 0.90) is added, with stirring. The crystals are collected at once on the filter, washed with 200 cc. of water, and allowed to dry in the air. The yield is 240 g. (84 per cent of the theoretical amount) of a light yellow product, melting at 64–65°. This material may be used without further purification (and without being dried) for the preparation of orthanilic acid.

(*B*) *Orthanilic Acid.*—A 3-l. flask is fitted with a reflux condenser and a liquid-sealed stirrer, and is placed on a hot plate. In the flask is placed a mixture of 200 g. (0.90 mole) of *o*-nitrobenzenesulfonyl chloride, 100 g. of anhydrous sodium carbonate, and 600 cc. of water. The mixture is heated to boiling and stirred in order to promote the hydrolysis, which is complete within forty-five minutes after the compound has melted. The orange-red solution is filtered, and the filtrate is made just acid to litmus by the addition of acetic acid, about 25 cc. being required. The solution is transferred to a 3-l. three-necked flask which is provided with a reflux condenser and an efficient liquid-sealed stirrer. The solution is heated to boiling on the hot plate, and iron filings (about 20-mesh) are added, with vigorous stirring, at the rate of about 25 g. every fifteen minutes. A total of 350 g. of iron is used. In a few minutes the mixture becomes very deep brown in color and has a tendency to foam. After stirring for four hours, a sample when filtered should yield an almost colorless filtrate; if the filtrate is red or orange, stirring and heating must be continued. When a light-colored filtrate is obtained, 2 g. of decolorizing carbon is added, the hot mixture is filtered by suction, and the residue is washed several times with small amounts of hot water which are added to the main solution. The filtrate is chilled to about 15°, and 95 cc. of concentrated hydrochloric acid is slowly added. The orthanilic acid separates in fine colorless crystals which appear as hexagonal plates under the microscope (Note 1). When the temperature has again fallen to about 15°, the mass is filtered and the precipitate is washed with water and then with ethyl alcohol. If about 20 cc. of concentrated hydrochloric acid is added to the filtrate, an additional deposit of about 1 g. will be obtained after a few hours' standing. The yield is 89 g. (57 per cent of the theoretical amount). The compound is 97–100 per cent pure and for many purposes will not require recrystallization. Material of analytical purity may be obtained by one recrystallization from hot water. The decomposition point is about 325° (bloc Maquenne).

2. Notes

1. Solutions of orthanilic acid, when chilled below 13.5°, yield the hydrated form of the acid, which crystallizes as needles (see photographs in the paper by Fierz and others).[1]

3. Methods of Preparation

Orthanilic acid was first made by the reduction of nitrobenzenesulfonic acid by ammonium sulfide.[2] This reduction has also been carried out electrolytically, and by the use of iron or zinc.[3] The acid has also been made by the rearrangement of phenylsulfamic acid,[4] by the action of sodium hypobromite upon potassium *o*-carbaminebenzenesulfonate,[5] by the reduction of the mixed nitrobenzenesulfonic acids followed by separation of the isomers,[6] by the action of methyl alcohol upon *o*-nitrophenylsulfurchloride,[7] by the action of acid upon diacetyl diphenylsulfamide,[8] by the debromination of *p*-bromoaniline-*o*-sulfonic acid,[9] by the reduction of 1,2,6-aminothiophenolsulfonic acid,[10] and by the hydrolysis and reduction of *o*-nitrobenzenesulfonyl chloride, which was obtained from di-*o*-nitrophenyldisulfide.[11]

[1] Fierz, Schlittler, and Waldemann, Helv. Chim. Acta **12**, 663 (1929).
[2] Limpricht, Ann. **177**, 79, 98 (1875).
[3] Wohlfahrt, J. prakt. Chem. **66**, 556 (1902); Goldschmidt and Eckart, Z.

physik. Chem. **56**, 411 (1906); Holleman and Polak, Rec. trav. chim. **29**, 419 (1910); Sharvin, Arbuzov and Varshavskii, J. Chem. Ind. (Moscow) **6**, 1409 (1929).

[4] Bamberger and Hindermann, Ber. **30**, 654 (1897); Bamberger and Kunz, ibid. **30**, 2276 (1897); Bretschneider, J. prakt. Chem. [2] **55**, 286 (1897); Bamberger, Ber. **34**, 249 (1901); Baumgarten, ibid. **59**, 1976 (1926).

[5] Bradshaw, Am. Chem. J. **35**, 339 (1906).

[6] Bahlmann, Ann. **186**, 307 (1877); Franklin, Am. Chem. J. **20**, 457 (1898); Ger. pat. 281,176 [Frdl. **11**, 125 (1912–1914)].

[7] Zincke and Farr, Ann. **391**, 59 (1912).

[8] Wohl and Koch, Ber. **43**, 3301 (1910).

[9] Thomas, Ann. **186**, 128 (1877); Ger. pat. 84,141 [Frdl. **4**, 90 (1894)]; Kreis, Ann. **286**, 377 (1895); Bradshaw, Am. Chem. J. **35**, 340 (1906); Boyle, J. Chem. Soc. **95**, 1698 (1909); Scott and Cohen, ibid. **121**, 2042 (1922).

[10] Rassow and Döhle, J. prakt. Chem. [2] **93**, 188, 203 (1916).

[11] Elgersma, Rec. trav. chim. **48**, 752 (1929).

XXI

PHENYLARSONIC ACID

$$C_6H_5NH_2 + 2HCl + NaNO_2 \rightarrow C_6H_5N_2Cl + 2H_2O + NaCl$$

$$C_6H_5N_2Cl + Na_3AsO_3 \xrightarrow{(CuSO_4)} C_6H_5AsO_3Na_2 + N_2 + NaCl$$

$$C_6H_5AsO_3Na_2 + 2HCl \rightarrow C_6H_5AsO_3H_2 + 2NaCl$$

Submitted by R. H. Bullard and J. B. Dickey.
Checked by Wallace H. Carothers and W. L. McEwen.

1. Procedure

In a 12-l. round-bottomed flask fitted with a mechanical stirrer is placed 1 l. of water. The water is heated to boiling and 500 g. (4.7 moles) of anhydrous sodium carbonate is added. As soon as the carbonate has dissolved, 250 g. (1.26 moles) of arsenious oxide and 11 g. of crystalline copper sulfate are added with stirring. When all the solids have dissolved the solution is cooled with stirring under a stream of tap water until the temperature falls to 15°.

Concurrently with the preparation of the sodium arsenite solution, a solution of benzenediazonium chloride is prepared. To a well stirred mixture of 186 g. (2.0 moles) of technical aniline, 400 cc. (4.8 moles) of concentrated hydrochloric acid (sp. gr. 1.19), 1 l. of water, and enough crushed ice to make a volume of about 3 l. is added slowly a solution of 145 g. (2.0 moles) of 95 per cent sodium nitrite in 500 cc. of water. This requires about thirty to forty minutes.

The benzenediazonium chloride solution is then added with stirring during a period of one hour to the suspension of sodium arsenite, cooled in an ice and salt bath to 0°. The temperature during the reaction is held below 5° (Note 1). Frothing takes place owing to the escape of nitrogen, but this is easily controlled

by the occasional addition of a small quantity of benzene. Stirring is continued for one hour after the addition of the diazonium chloride solution, and the mixture is filtered to remove the solid material which separates. This is washed with 500 cc. of cold water, and the combined liquors are concentrated over a free flame to a volume of about 1.5 l. (Note 2).

To the hot concentrated solution, which is deep brown in color, concentrated hydrochloric acid is added until no more tarry material separates (Note 3). The tar is filtered and more hydrochloric acid is added until after filtering a clear, pale yellow solution results. It is important to remove all the tar at this time; otherwise, subsequent recrystallizations will not free the product from color. The phenylarsonic acid is then precipitated by the addition of 250 cc. of concentrated hydrochloric acid (sp. gr. 1.19) (Note 4). When the mixture has cooled (preferably by standing overnight) the phenylarsonic acid is filtered on a Büchner funnel and washed with 200 cc. of cold water. The light yellow crystals are dissolved in 500 cc. of boiling water, 20 g. of decolorizing carbon (Norite) added, the solution filtered hot and the filtrate allowed to cool. After filtering and drying, the white crystals melt with decomposition at 154–158°, passing into the anhydride, $C_6H_5AsO_2$. The yield is 160–182 g. (39–45 per cent of the theoretical amount) (Note 5).

2. Notes

1. This temperature is advised because it appears to be near the optimum with regard to yield and ease of purifying the product. However, a reaction temperature as high as 15° may be used with good results.

2. The solution is concentrated at atmospheric pressure since frothing occurs if reduced pressure is used.

3. About 100 cc. of hydrochloric acid is required. Care must be exercised not to throw out any of the phenylarsonic acid.

4. Too large an excess of hydrochloric acid will dissolve some of the product and lower the yield.

5. In occasional runs by this procedure yields as high as 57 per cent have been obtained but the reasons for this are not known.

3. Methods of Preparation

Phenylarsonic acid has been prepared by oxidizing phenyldichloroarsine [1] or phenyldiiodoarsine [2] with chlorine in water; by the oxidation of phenylarsine with nitric acid or air;[3] by decomposing phenylarsinetetrachloride or phenylarsineoxychloride with water;[4] by heating iodobenzene or bromobenzene with potassium arsenite;[5] by diazotizing *p*-arsanilic acid and decomposing in a solution of sodium hydrosulfite and hydrochloric acid;[6] by the action of potassium arsenite on potassium benzene-isodiazo oxide;[7] by the action of benzenediazonium chloride on sodium arsenite in the presence of a copper compound [8] or of magnesium chloride and copper powder;[9] by the action of a neutral or alkaline mixture containing arsenious oxide, a copper salt, and a reducing agent on benzenediazonium chloride.[10]

The preparation given here in detail is essentially that described by Adams and Palmer.[8]

[1] Michaelis and Loesner, Ber. **27**, 265 (1894); Rosenheim and Bilecki, ibid. **46**, 551 (1913); Roeder and Blasi, ibid. **47**, 2752 (1914).

[2] Bertheim, ibid. **47**, 274 (1914).

[3] Palmer and Dehn, ibid. **34**, 3599 (1901); Dehn, Am. Chem. J. **33**, 149 (1905).

[4] Michaelis, Ber. **10**, 625 (1877); LaCoste and Michaelis, Ann. **201**, 203 (1880).

[5] Dehn, Am. Chem. J. **33**, 140 (1905); Rosenmund, Ber. **54**, 438 (1921).

[6] Bertheim, ibid. **41**, 1853 (1908).

[7] Bart, Ger. pat. 250,264 [Frdl. **10**, 1254 (1910–1912)].

[8] Ger. pat. 264,924 [Frdl. **11**, 1030 (1912–1914)]; Palmer and Adams, J. Am. Chem. Soc. **44**, 1361 (1922); Norris, J. Ind. Eng. Chem. **11**, 825 (1919); Schmidt, Ann. **421**, 169 (1920).

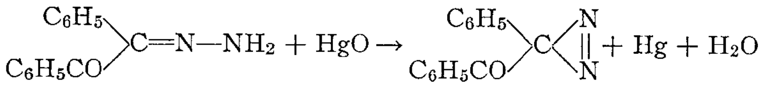
[9] Bart, Ger. pat. 254,092 [Frdl. **11**, 1030 (1912–1914)].

[10] Mouneyrat, Brit. pat. 142,947 [C. A. **14**, 2802 (1920)].

XXII

PHENYLBENZOYLDIAZOMETHANE

(Azibenzil)



Submitted by Costin D. Nenitzescu and Eugen Solomonica.
Checked by L. F. Fieser and Ralph S. Temple.

1. Procedure

Thirty grams (0.134 mole) of benzilhydrazone (Note 1) is mixed in a mortar with 60 g. (0.28 mole) of yellow mercuric oxide and 15 g. of anhydrous sodium sulfate (Note 2). The mixture is introduced into a 500-cc. glass-stoppered bottle and covered with 200 cc. of absolute ether (Note 3). Four cubic centimeters of a cold, saturated solution of alcoholic potassium hydroxide is added to catalyze the reaction (Note 4), and the mixture is shaken for ten to fifteen minutes. The solution is filtered by gravity through a fine paper, and the residue is washed several times with ether until the liquid is only slightly colored. The combined ethereal extracts are evaporated to dryness at the pressure of the water pump by heating the flask in a water bath to a temperature not greater than 40° (Note 5). The yellow, crystalline material is dried on a porous plate and recrystallized from anhydrous ether. The yield of azibenzil which melts at about 79° with decomposition is 26–28 g. (87–94 per cent of the theoretical amount) (Note 6).

2. Notes

1. Benzil hydrazone [1] may be prepared as follows:[2] A mixture of 52 g. (0.4 mole) of hydrazine sulfate (Org. Syn. Coll. Vol. **1**, 302), 110 g. (0.8 mole) of sodium acetate, and 250 g. of

water is boiled five minutes, cooled to about 50°, and 225 cc. of methyl alcohol added. The precipitated sodium sulfate is filtered and washed with a little alcohol.

A hot solution of 50 g. (0.24 mole) of benzil (Org. Syn. Coll. Vol. **1**, 80) in 75 cc. of methyl alcohol is prepared, and the above solution, heated to 60°, is added. Most of the benzil hydrazone separates immediately, but the yield is increased by refluxing a half hour. The hydrazone is filtered from the cold solution and washed with a little ether to remove the yellow color. The yield is 50.5 g. (94 per cent of the theoretical amount), melting at 147–151° with decomposition.

2. The sodium sulfate absorbs the water formed during the reaction.

3. By using ether instead of benzene or petroleum ether, as specified in the older methods, the evaporation of the solvent after the reaction is facilitated.

4. Without this catalyst the oxidation may require several hours, and the results vary considerably and depend largely upon the quality of the mercuric oxide.

5. The material may explode if the evaporation is carried out at atmospheric pressure on the steam bath.

6. This procedure may be used also for the preparation of diazofluorene.[3]

3. Methods of Preparation

Phenylbenzoyldiazomethane has been prepared by the oxidation of benzilhydrazone with mercuric oxide,[4] using benzene or petroleum ether as the solvent, and without the catalyst here specified.

[1] Curtius and Thun, J. prakt. Chem. [2] **44**, 176 (1891).
[2] Private communication from C. F. H. Allen.
[3] Staudinger and Kupfer, Ber. **44**, 2207 (1911); Staudinger and Gaule, ibid., **49**, 1955 (1916).
[4] Curtius and Thun, J. prakt. Chem. [2] **44**, 182 (1891).

XXIII

γ-PHENYLBUTYRIC ACID

$$C_6H_5COCH_2CH_2COOH + 4[H](Zn + HCl) \rightarrow C_6H_5CH_2CH_2CH_2COOH + H_2O$$

Submitted by S. C. OVERBAUGH, C. F. H. ALLEN, E. L. MARTIN, and L. F. FIESER.
Checked by C. R. NOLLER.

1. Procedure

A MIXTURE of 100 g. (1.53 gram atoms) of amalgamated zinc (Note 1), 50 g. (0.28 mole) of β-benzoylpropionic acid (p. 92), and 250 cc. of concentrated hydrochloric acid (sp. gr. 1.18) is placed in a 1-l. round-bottomed flask fitted with a reflux condenser and a gas trap (Org. Syn. **14**, 2) (Note 2), and refluxed briskly for nine hours (Note 3). Then 100 cc. of concentrated hydrochloric acid is added and the refluxing continued for an additional hour. On cooling to room temperature, the γ-phenylbutyric acid solidifies and is collected on a Büchner funnel and washed with 500 cc. of cold water. The filtrate and the washings are combined and extracted three times with 75-cc. portions of ether. The acid collected on the funnel is added to the combined extract and dissolved by shaking. The solution is filtered to remove a small amount of insoluble product (Note 4) which is washed with two 10-cc. portions of ether, and the combined filtrate is dried with anhydrous calcium chloride. The solvent is removed and the acid is distilled at reduced pressure. The yield of product boiling at 148–154°/8–10 mm. or 125–130°/3 mm. is 33–36 g. (72–78 per cent of the theoretical amount). It is a colorless oil which crystallizes to a white solid on cooling and melts at 46–48° (Note 5).

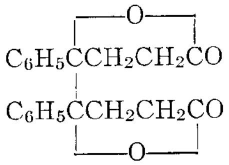
2. Notes

1. The amalgamated zinc is prepared by adding 100 g. of mossy zinc to a solution of 10 g. of mercuric chloride in 200 cc. of water and shaking for one-half hour. The liquid is then poured off and the metal washed by decantation.

2. Considerable hydrogen chloride is driven off during the initial heating, and it might appear that it would be advantageous to use constant-boiling instead of concentrated hydrochloric acid. If this is done, however, the product has a melting point of 40–44° and the yield is somewhat lower.

3. If the refluxing is interrupted for any reason, great care must be exercised to avoid frothing on heating again. The upper part of the flask may be occasionally brushed with a free flame. Once the two layers are well mixed, boiling proceeds smoothly.

4. This solid, m.p. 254°, is a reduction product of unreported structure and weighs 1–2 g. Unpublished work by L. F. Fieser indicates that it has the formula



being evidently the result of a pinacol reduction.

5. The recorded melting points vary from 47° to 51°. The acid may be crystallized from hot water (75 cc. per g.) but the recovery is only about 50 per cent. No other suitable solvent or combination of solvents was discovered. Redistillation raises the melting point to 47–48° with only mechanical losses.

3. Methods of Preparation

Of the several methods by which γ-phenylbutyric acid has been obtained, those of preparative value are decarboxylation of γ-phenylethylmalonic acid;[1] carbonation of γ-phenylpropylmag-

nesium bromide;[2] and reduction of β-benzoylpropionic acid with amalgamated zinc and hydrochloric acid[3] or of its hydrazone with sodium methylate.[4]

[1] Fischer and Schmitz, Ber. **39**, 2212 (1906).
[2] Grignard, Compt. rend. **138**, 1049 (1904); Rupe and Proske, Ber. **43**, 1233 (1910).
[3] Krollpfeiffer and Schäfer, ibid. **56**, 620 (1923).
[4] Staudinger and Müller, ibid. **56**, 713 (1923).

XXIV

PHENYLGLYOXAL

$$C_6H_5COCH_3 + SeO_2 \rightarrow C_6H_5COCHO + Se + H_2O$$

Submitted by H. A. Riley and A. R. Gray.
Checked by L. F. Fieser and C. H. Fisher.

1. Procedure

In a 1-l. three-necked, round-bottomed flask fitted with a liquid-sealed stirrer and a reflux condenser are placed 600 cc. of dioxane (Note 1), 111 g. (1 mole) of selenium dioxide (Note 2), and 20 cc. of water (Note 3). The mixture is heated to 50–55° and stirred until the solid has gone into solution, 120 g. (1 mole) of acetophenone is added in one lot, and the resulting mixture is refluxed with continued stirring for four hours (Note 4). The hot solution is decanted from the precipitated selenium, and the dioxane and water are removed by distillation through a short column. The phenylglyoxal is distilled at diminished pressure from a 250-cc. Claisen flask (Note 5), and the fraction boiling at 95–97°/25 mm. collected (Note 6). The yield is 93–96 g. (69–72 per cent of the theoretical amount) (Note 7).

The aldehyde sets to a stiff gel on standing, probably as the result of polymerization. It may be recovered without appreciable loss by distillation. Phenylglyoxal may be preserved also in the form of the hydrate, which is conveniently prepared by dissolving the yellow liquid in 3.5–4 volumes of hot water and allowing crystallization to take place (Note 8).

2. Notes

1. Ethyl alcohol (95 per cent) can also be used as solvent. The reaction can be carried out with an excess of acetophenone

(2 moles) as solvent, but the results are less satisfactory. The dioxane can be recovered and used in later runs.

2. For the preparation of selenium dioxide 200 g. (141 cc.) of concentrated nitric acid is heated in a 3-l. beaker on a hot plate under a good hood and 100 g. of selenium is added in portions of 5–10 g. A glass mechanical stirrer to break the foam hastens the process of oxidation. The resulting solution is transferred under the hood to a large evaporating dish and heated on a hot plate at a temperature not exceeding 200° until the selenious acid is completely dehydrated. The crude product is purified by sublimation. A 50-g. portion of the oxide is transferred to a 7-cm. porcelain crucible upon which is placed a 250-cc. filter flask through which a stream of cold water is run from the tap. The crucible is protected with asbestos and heated with a low flame until sublimation is complete (20–30 minutes). When the crucible has cooled, the sublimed selenium dioxide will be found wedged against the condenser. Extreme care should be used when working with selenium dioxide because of its poisonous properties.

3. Commercial selenious acid (129 g., 1 mole) may be used in place of the mixture of selenium dioxide and water.

4. After about two hours the solution becomes clear and little further precipitation of selenium is observable.

5. Several grams of the hydrate may be obtained by adding the fore-run to an equal volume of warm water and allowing the product to crystallize.

6. Boiling points reported in the literature are 120°/50 mm. and 142°/125 mm.

7. Phenylacetaldehyde may be used in place of acetophenone. Phenylmethylglyoxal is obtained in a similar manner from propiophenone, and in a large number of cases compounds containing a methylene group adjacent to a carbonyl group may be oxidized by means of selenium dioxide to the corresponding α-ketoaldehyde or α-diketone.[1]

8. The solubility of the hydrate at 20° is given in the literature as 1 part in about 35 parts of water. The melting points recorded range from 73° to 91°; the difference is said to be due to varying degrees of dryness of the samples.[2] The hydrate crystallizes well from water; chloroform, carbon disulfide, alcohol, or ether-ligroin also may be used for the purpose. Phenylglyoxal can be recovered from the hydrate by distillation in vacuum.

3. Methods of Preparation

Phenylglyoxal has been prepared from isonitrosoacetophenone through the bisulfite compound [2,3] or by treatment with nitrosylsulfuric acid [4] or with nitrous acid.[5] It also has been prepared by the oxidation of benzoylcarbinol with copper acetate,[6] by heating bromophenacyl acetate,[7] and by the oxidation of acetophenone with selenium dioxide.[1]

[1] Riley, Morley, and Friend, J. Chem. Soc. **1932**, 1875; Brit. pat. 354,798 [C. A. **26**, 3804 (1932)].

[2] Pinner, Ber. **35**, 4132 (1902); ibid. **38**, 1532 (1905).

[3] v. Pechmann, ibid. **20**, 2904 (1887); Müller and v. Pechmann, ibid. **22**, 2556 (1889); Smedley, J. Chem. Soc. **95**, 218 (1909).

[4] Neuberg and Hofmann, Biochem. Z. **229**, 443 (1930).

[5] Neuberg and Hofmann, ibid. **239**, 495 (1931).

[6] Nef, Ann. **335**, 271 (1904); Henze, Z. physiol. Chem. **198**, 83 (1931); ibid. **200**, 232 (1931).

[7] Madelung and Oberwegner, Ber. **65**, 931 (1932).

XXV

PHLOROACETOPHENONE
(2,4,6-Trihydroxyacetophenone)

$$C_6H_3(OH)_3 + CH_3CN \xrightarrow{(ZnCl_2)} (HO)_3C_6H_2\underset{\displaystyle CH_3}{\underset{|}{C}}{=}NH\cdot HCl$$

$$(HO)_3C_6H_2\underset{\displaystyle CH_3}{\underset{|}{C}}{=}NH\cdot HCl + H_2O \longrightarrow (HO)_3C_6H_2COCH_3 + NH_4Cl$$

Submitted by K. C. Gulati, S. R. Seth, and K. Venkataraman.
Checked by John R. Johnson and M. T. Bush.

1. Procedure

In a 250-cc. filtering flask fitted with a calcium chloride tube and a rubber stopper carrying an inverted thistle tube (Note 1) for the introduction of hydrogen chloride, are placed 20 g. (0.16 mole) of well-dried phloroglucinol (Note 2), 13 g. (0.32 mole) of anhydrous acetonitrile, 80 cc. of anhydrous ether, and 4 g. of finely powdered, fused zinc chloride. The flask is cooled in an ice-salt mixture and shaken occasionally while a rapid stream of dry hydrogen chloride (Org. Syn. Coll. Vol. **1**, 520) is passed through the solution for two hours. The flask is allowed to stand in an ice chest for twenty-four hours and hydrogen chloride is again passed into the mixture, now pale orange in color, for two hours. The flask is stoppered and allowed to stand in an ice chest for three days.

The bulky orange-yellow precipitate of the ketimine hydrochloride is separated by decanting the ether and washed twice with 20-cc. portions of dry ether. The solid is transferred to a 2-l. round-bottomed flask with 1 l. of hot water. The flask is provided with a reflux condenser, and the yellow solution is boiled vigorously over a wire gauze for two hours. A small quantity (3–4 g.) of decolorizing carbon (Norite) is added, the

solution boiled for five minutes longer and filtered with suction while hot. The decolorizing carbon is extracted with two 100-cc. portions of boiling water and this filtrate added to the main portion.

After standing overnight the colorless or pale yellow needles of phloroacetophenone are filtered with suction and dried in an oven at 120° (Note 3). The yield is 20–23.5 g. (74–87 per cent of the theoretical amount) of a product which melts at 217–219° (corr.). This product is quite pure and may be used directly for many purposes. It may be recrystallized from thirty-five times its weight of hot water, with a loss of about 5 per cent. The recrystallized material melts at 218–219° (corr.).

2. Notes

1. A wide-mouthed entry tube for hydrogen chloride is necessary to avoid clogging due to separation of the solid ketimine hydrochloride.

2. All the reagents must be dried carefully. Ordinary phloroglucinol contains two molecules of water of hydration, which is removed by drying overnight at 120°. The acetonitrile and ether used were freshly distilled from phosphorus pentoxide.

3. Phloroacetophenone crystallizes from aqueous solutions with one molecule of water of hydration.[1] The oven-dried crystals take up water readily on exposure to the air. Phloroacetophenone gives a wine-red color with ferric chloride in contrast to the violet color given by phloroglucinol.[2]

3. Methods of Preparation

The Hoesch reaction is the most satisfactory method for preparing phloroacetophenone.[3] The procedure described above is that of Robinson and Venkataraman.[4] Phloroacetophenone has been obtained also by the action of acetyl chloride on phloroglucinol in the presence of aluminum chloride.[2]

[1] Gulati, Seth, and Venkataraman, J. Chem. Soc. **1934**, 1766.
[2] Shriner and Kleiderer, J. Am. Chem. Soc. **51**, 1269 (1929).
[3] Hoesch, Ber. **48**, 1129 (1915).
[4] Robinson and Venkataraman, J. Chem. Soc. **1926**, 2347.

XXVI

n-PROPYL SULFIDE

$$C_2H_5ONa + H_2S \rightarrow NaSH + C_2H_5OH$$

$$NaSH + C_2H_5ONa \rightarrow Na_2S + C_2H_5OH$$

$$Na_2S + 2CH_3CH_2CH_2Br \rightarrow (CH_3CH_2CH_2)_2S + 2NaBr$$

Submitted by R. W. Bost and M. W. Conn.
Checked by Reynold C. Fuson and Charles F. Woodward.

1. Procedure

In a 2-l. round-bottomed flask fitted with a reflux condenser and a 6-mm. glass tube closed at the upper end with a rubber tube and pinchcock and reaching to the bottom of the flask, are placed 800 cc. of absolute alcohol and 50.6 g. (2.2 gram atoms) of clean sodium cut in small pieces. When the sodium is completely dissolved, one half of the solution is transferred to a 2-l. three-necked, round-bottomed flask fitted with a dropping funnel, a liquid-sealed mechanical stirrer, and a reflux condenser closed by a calcium chloride tube. The flask containing the remainder of the solution is connected again to the reflux condenser, and hydrogen sulfide from a cylinder is introduced by means of the glass tube at the rate of about two bubbles per second until the solution is saturated (about six hours is required). This solution of sodium hydrogen sulfide is added to that of sodium ethylate in the three-necked flask and the mixture refluxed for one hour. After cooling to room temperature, sufficient absolute alcohol (about 200 cc.) is added to dissolve all the sodium sulfide.

To this solution of sodium sulfide is added dropwise with stirring 246 g. (2 moles) of *n*-propyl bromide (Org. Syn. **13**, 21). After all the bromide has been added the flask is heated on a steam cone for eight hours (Note 2), during which time the mix-

ture should not be stirred too vigorously. It is then cooled and added to 2 l. of 25 per cent aqueous sodium chloride solution contained in a separatory funnel. The mixture is shaken to insure thorough mixing, allowed to stand until the layers have separated, and the upper oily layer of propyl sulfide removed and dried with anhydrous sodium sulfate. The lower layer is extracted with five 200-cc. portions of petroleum ether (b.p. 25–45°) (Note 3), the extract dried with 20 g. of sodium sulfate, and the petroleum ether distilled through a 60-cm. fractionating column until the temperature of the vapors passing over reaches 60°. The residue is added to the crude propyl sulfide previously separated and the combined portions distilled. The yield of product boiling at 140–143° is 80–100 g. (69–86 per cent of the theoretical amount) (Note 4).

2. Notes

1. It is best to have the sodium sulfide completely dissolved before it is added to the bromide; subsequent extraction is facilitated, however, if the solution is kept at a minimum volume.

2. In order to be certain that no propyl sulfide is being lost during the refluxing, the condenser should be connected to a trap containing an aqueous solution of mercuric chloride. Condenser water cooled to 5–10° is recommended.

3. To avoid contamination of the product the petroleum ether should be distilled before being used. Ethyl ether is not suitable for this extraction.

4. *n*-Butyl and *sec.*-amyl sulfides can be prepared by procedures essentially the same as that given here.

3. Methods of Preparation

n-Propyl sulfide has always been prepared by the action of an alcoholic solution of an alkali sulfide on *n*-propyl halides.[1]

[1] Cahours, Compt. rend. **76**, 133 (1873); Winssinger, Bull. soc. chim. [2] **48**, 109 (1887).

XXVII

REINECKE SALT

$NH_4[Cr(NH_3)_2(SCN)_4] \cdot H_2O$

Submitted by H. D. Dakin.
Checked by H. T. Clarke and R. S. Ingols.

1. Procedure

Eight hundred grams of ammonium thiocyanate (10.5 moles) is gently heated, by means of three small flames (Note 1), in a white enameled cooking pot of about 4 l. capacity. The mass is stirred with a thermometer enclosed in a glass tube until it has partially melted and the temperature has reached 145–150°. At this point an intimate mixture of 170 g. (0.675 mole) of finely powdered ammonium dichromate and 200 g. of ammonium thiocyanate (2.6 moles) is added in portions of 10–12 g. with constant stirring. After about ten such portions have been added a fairly vigorous reaction takes place with evolution of ammonia and the temperature rises to 160°. The flames are extinguished and the remainder of the mixture is added at such a rate that the heat of reaction maintains the temperature at 160° (Note 2). Stirring is continued while the mass cools, care being taken to detach lumps of solid which form around the sides of the vessel (Note 3).

The product, while still warm (Note 4), is finely powdered and stirred with 750 cc. of ice water in a large beaker. After fifteen minutes the insoluble portion is filtered by suction, freed as completely as possible from mother liquor without washing (Note 5), and stirred into 2.5 l. of water previously warmed to 65°. The temperature is then rapidly raised to 60° (Note 6), the solution

is filtered at once through a hot-water funnel, and the filtrate placed in a refrigerator overnight.

The resulting crystals are collected and the mother liquor employed for a second similar extraction of the residue at 60°. This yields a further crop of crystalline Reinecke salt. The mother liquor is finally concentrated to 250–300 cc. by evaporation at 40–50° under reduced pressure, when a small third crop (12–13 g.) is obtained. The total yield of air-dried crystals is 250–275 g. (52–57 per cent of the theoretical amount) (Note 7).

The undissolved residue from the second extraction consists chiefly of Morland salt (the guanidine salt of the Reinecke acid) and amounts to 130–135 g. (33–34 per cent of the theoretical amount) (Note 8).

2. Notes

1. Heat must be applied as uniformly as possible.
2. The addition of the mixture requires five to seven minutes.
3. The product is detached from the walls during cooling as it is difficult to remove when cold.
4. The material should be pulverized while warm before it has had an opportunity to attract moisture from the air.
5. The filtrate, which consists largely of unchanged ammonium thiocyanate and its decomposition products, contains too little Reinecke salt to repay further treatment.
6. Reinecke salt decomposes in aqueous solution with formation of a blue color and free hydrogen cyanide. At room temperature this decomposition occurs in about two weeks, and above 65° it takes place quite rapidly. A similar decomposition takes place in boiling alcohol.
7. Reinecke salt is of value as a precipitant for primary and secondary amines, proline and hydroxyproline, and certain amino acids.[1]
8. The Morland salt, which is soluble in acetone, contains a small proportion of a colorless sulfur compound insoluble in hot water. It can be partially converted into Reinecke salt by treatment in dilute ammonia solution with a large excess of ammonium chloride, but the amounts so obtainable are unprofitably small.

3. Methods of Preparation

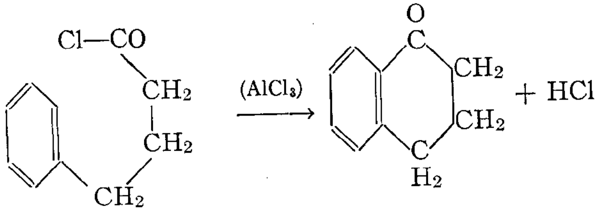
Reinecke salt has been prepared by adding either potassium dichromate [2] or ammonium dichromate [1,3] to fused ammonium thiocyanate.

[1] Kapfhammer and Eck, Z. physiol. Chem. **170**, 294 (1927); Grassmann and Lang, Biochem. Z. **269**, 223 (1934).
[2] Reinecke, Ann. **126**, 113 (1863); Christensen, J. prakt. Chem. [2] **45**, 213 (1892); Zeleney and Gortner, J. Biol. Chem. **90**, 430 (1931).
[3] Werner, Z. anorg. Chem. **15**, 249 (1897); Ann. **406**, 276 (1914).

XXVIII

α-TETRALONE
(α-Ketotetrahydronaphthalene)

$$C_6H_5(CH_2)_3CO_2H + SOCl_2 \rightarrow C_6H_5(CH_2)_3COCl + HCl + SO_2$$



Submitted by E. L. Martin and L. F. Fieser.
Checked by C. R. Noller.

1. Procedure

In a 500-cc. round-bottomed flask fitted with a reflux condenser carrying at the top a tube leading to a gas absorption trap (Org. Syn. **14**, 2) are placed 32.8 g. (0.2 mole) of γ-phenylbutyric acid (p. 64) and 20 cc. (32 g., 0.27 mole) of thionyl chloride (Note 1). The mixture is carefully heated on a steam bath until the acid is melted and then the reaction is allowed to proceed without the application of external heat. After twenty-five to thirty minutes hydrogen chloride is no longer evolved and the mixture is warmed on the steam bath for ten minutes. The flask is then connected to the water pump, evacuated, and heated for ten minutes on the steam bath and finally for two or three minutes over a small flame in order to remove the excess thionyl chloride. The acid chloride thus obtained is a nearly colorless liquid and needs no further purification. The flask is cooled, 175 cc. of carbon disulfide is added, and the solution cooled in an ice bath. Thirty grams (0.23 mole) of

aluminum chloride is added rapidly in one lot, and the flask is immediately connected to the reflux condenser. After a few minutes, the rapid evolution of hydrogen chloride ceases and the mixture is slowly warmed to the boiling point on the steam bath. After heating and shaking the mixture for ten minutes the reaction is complete. The reaction mixture is cooled to 0° and the aluminum chloride complex is decomposed by the careful addition with shaking of 100 g. of ice. Twenty-five cubic centimeters of concentrated hydrochloric acid is added and the mixture transferred to a 2-l. round-bottomed flask and steam-distilled (Note 2). The carbon disulfide distils first (Note 3), and there is no difficulty in telling when to change the receiver for the collection of the α-tetralone for there is a definite break in the distillation. The reaction product comes over completely in about 2 l. of the next distillate. The oil is separated and the water is extracted three times with 100-cc. portions of benzene. The oil and extracts are combined, the solvent is removed, and the residue is distilled at reduced pressure. The yield of α-tetralone boiling at 105–107°/2 mm. is 21.5–26.5 g. (74–91 per cent of the theoretical amount based on the γ-phenylbutyric acid).

2. Notes

1. The thionyl chloride was purified by distilling 50 g. of commercial thionyl chloride from 10 cc. of quinoline and then from 20 cc. of boiled linseed oil in a system protected from moisture.

2. It is advisable to use an efficient condenser system, such as that described in Org. Syn. Coll. Vol. 1, 467, as α-tetralone is only moderately volatile with steam.

3. On recovery of the carbon disulfide there is not more than a trace of residue.

3. Methods of Preparation

α-Tetralone has been obtained by the oxidation of tetralin either catalytically [1] or by the use of chromic anhydride,[2] as a product of the catalytic hydrogenation of α-naphthol;[3] from

γ-phenylbutyryl chloride and aluminum chloride with yields of 10 per cent in petroleum ether solution [4] and 70 per cent in benzene solution;[5] and by the dehydration of γ-phenylbutyric acid with concentrated sulfuric acid in 27–50 per cent yields.[6]

[1] Ger. pat. 539,476 [C. A. **26**, 1614 (1932)].

[2] Ger. pat. 346,948 [Chem. Zentr. **93**, II, 114 (1922)].

[3] Ger. pat. 352,720 [C. A. **17**, 1245 (1923)].

[4] Kipping and Hill, J. Chem. Soc. **75**, 144 (1899).

[5] Amagat, Bull. soc. chim. [4] **41**, 940 (1927).

[6] Krollpfeiffer and Schäfer, Ber. **56**, 624 (1923); Horne and Shriner, J. Amer. Chem. Soc. **55**, 4652 (1933); Cook and Hewett, J. Chem. Soc., **1934**, 373.

XXIX

TRICHLOROETHYL ALCOHOL

$$3CCl_3CHO + Al(OCH_2CH_3)_3 \rightarrow 3CH_3CHO + Al(OCH_2CCl_3)_3$$

$$2Al(OCH_2CCl_3)_3 + 3H_2SO_4 \rightarrow Al_2(SO_4)_3 + 6CCl_3CH_2OH$$

Submitted by WILLIAM CHALMERS.
Checked by REYNOLD C. FUSON and H. H. HULLY.

1. Procedure

IN a 2-l. three-necked flask immersed in an oil bath are placed 250 g. (1.7 moles) of anhydrous chloral, 650 cc. of anhydrous alcohol (Note 1), and 75 g. (0.64 mole) of pure aluminum ethylate (Note 2). An efficient fractionating column (Note 3) is attached to the flask through a cork in the central neck, and through one of the side necks is passed a tube leading to the bottom of the flask for the introduction of dry nitrogen. The remaining neck is tightly stoppered. It is used to withdraw portions of liquid for testing.

To the outlet of the column is attached a U-tube and a Peligot tube each of about 100-cc. capacity. The U-tube is immersed in a freezing mixture and the Peligot tube is filled with saturated sodium bisulfite solution. The oil bath is then heated to 135° and a slow current of gas is admitted. The mixture boils vigorously but the alcohol is returned by the refluxing device whereas the acetaldehyde formed by the reaction is allowed to pass through and is caught in the freezing mixture and the Peligot tube.

The end of the reaction is easily determined by removing a few drops of the reaction mixture and treating with water in a test tube. After the aluminum hydroxide settles, the clear liquid is decanted and a few drops of yellow ammonium sulfide are

added to it. So long as chloral is present, even in traces, a dark brown coloration will be produced on heating to incipient boiling. If the liquid collecting in the U-tube be removed every few hours, the completion of the reaction will be readily noticed by the diminishing quantity of acetaldehyde coming over. After twenty-three or twenty-four hours of heating (over a period of two or three days) the reaction is complete. The temperature of the bath is then allowed to fall to 120° and the alcohol is distilled through an ordinary condenser which replaces the fractionating column. When the residue of aluminum trichlorethylate is nearly dry (Note 5), the flask is removed from the oil bath and the solid is treated with 250 cc. of 20 per cent sulfuric acid and stirred thoroughly to insure complete decomposition.

The mixture is then subjected to steam distillation until no more trichloroethyl alcohol passes over. About 4 l. of distillate is obtained (Note 6). The oil is separated from the aqueous layer and the latter is salted out by saturating with sodium sulfate and extracted with three 200-cc. portions of ether. The ether solution is added to the main portion of the alcohol and the whole is dried over anhydrous sodium sulfate.

The ether is removed by distillation and the product distilled under reduced pressure (Note 7). There is obtained 215 g. (84 per cent of the theoretical amount) of trichloroethyl alcohol boiling at 94–97°/125 mm. and melting at 16–17° (Note 8). A purer compound can be obtained by refractionation under reduced pressure and pressing out the crystals on a cooled porous plate. Pure trichloroethyl alcohol has a melting point of 19° (Note 9).

2. Notes

1. The action of a small proportion of aluminum ethylate on pure chloral or chloral diluted with benzene leads to the formation of trichloroethyl trichloroacetate in the same manner that ethyl acetate is formed from acetaldehyde by aluminum ethylate, but the yields are small. A slightly better yield is obtained when molecular proportions are employed, but it is only in the presence of a large amount of an alcohol that good yields are obtained.

2. Aluminum ethylate is now obtainable commercially. The author recommends the following method of preparation[1] which has been checked:

In a flask fitted with a reflux condenser is placed 27 parts of aluminum filings or groats. This is treated with 276 parts of absolute alcohol and 0.1 to 0.25 part of mercuric chloride and several crystals of iodine. After a few minutes a violent evolution of hydrogen takes place, and by heating on the water bath for several hours the ethylate is produced in the form of a grayish powder.

Unchanged alcohol is removed by distillation from an oil bath until the residual material melts to a dark-colored liquid. It is then poured into a Claisen flask and distilled under reduced pressure, using a short air condenser and a Pyrex suction-flask as a receiver. Since aluminum ethylate tends to sublime, a glass-wool filter is inserted between the receiving flask and the vacuum line to prevent clogging. A free flame is necessary and distillation should be rapid. While the distillate is still liquid it is poured into a Pyrex flask and allowed to cool. It forms a tough, white mass which must be preserved in a well-stoppered flask to prevent adsorption of water vapor. A yield of 90 per cent of the theoretical amount may be obtained.

For the present reaction, where a trace of water does no harm, some of the ethylate may be fused and poured into a mortar and covered with a watch-glass until cool, when it can be powdered and weighed.

The submitter has found that it is possible to make a large quantity of the ethylate using the above method with 95 per cent alcohol, but that success is more certain if the alcohol be refluxed and distilled twice over quicklime.

3. This column must be capable of separating acetaldehyde from ethyl alcohol with the greatest completeness. A very efficient type is that of Hahn,[2] in which the column is kept at a constant temperature by means of boiling methyl alcohol in a central tube, the vapors passing up an outer annular space. It is necessary that the lower part of the condenser employed be sufficiently broad (say 2 cm. in diameter) so that when in

operation there will be no tendency for liquid to collect in the column.

A column involving the same principle can be made from two reflux condensers. The lower outlet of the outer jacket of the condenser connected to the flask is closed, and the jacket is filled to about two-thirds its height with methyl alcohol. A few small pieces of pumice are introduced to prevent bumping of the alcohol. The upper outlet of this jacket is joined to a second condenser to prevent loss of the methanol vapors. The inner tube of the fractionating column is filled with glass beads which are held in place by indentations made in the lower part of the tube. The outlet of this tube is connected to the U-tube immersed in the freezing mixture.

Care is essential to insure the complete separation of aldehyde and alcohol because of the fact that any slight continual loss of solvent is multiplied into a serious loss in the long period of heating necessary. The boiling point of chloral is only twenty degrees above that of ethyl alcohol and any loss of the latter would lead to some loss of the reagent.

4. The nitrogen is supplied from a cylinder and is dried by passing through a calcium chloride tube and a tube containing phosphorus pentoxide mixed with glass wool or beads. A tube filled with glass wool is placed between the phosphorus pentoxide tube and the flask to prevent the pentoxide from being blown into the reaction mixture if the nitrogen is turned on too rapidly.

5. Care should be taken that the residue is not heated too strongly as it becomes compact and some tarry material is formed which makes the action of the acid upon it very slow.

6. A small amount of trichloroaldol, $CCl_3 \cdot CHOH \cdot CH_2 \cdot CHO$, can be extracted from the residue of the steam distillation by means of ether.

7. The product can be distilled at ordinary pressure at a temperature of 151° but the distillate has a brown color due to slight decomposition.

8. Even by simple refluxing of the mixture without separation of the aldehyde, a yield of 65 per cent may be obtained.[3] The reaction between the aluminum ethylate and the chloral is in

equilibrium with that between the aluminum trichlorethylate and the acetaldehyde. A certain amount of the acetaldehyde is removed from the reaction by condensation to ethyl acetate under the catalytic influence of aluminum ethylate, but the change takes place only slowly in this mixture. A great deal of the aldehyde is converted into paraldehyde and acetal, but these changes are reversible.

9. The use of aluminum ethylate in the presence of alcohol offers a means of reducing many compounds which could not be reduced in the desired manner by the more customary methods. Meerwein and his students have used the method to convert bromal into tribromoethyl alcohol and have also prepared cinnamyl alcohol and various halogenated cinnamyl and crotyl alcohols from the corresponding aldehydes.[4,5] In all cases excellent yields are obtained.

3. Methods of Preparation

The method given here is essentially that of Meerwein and his pupils Schmidt [5] and von Bock.[3] The theory of the reaction and applications are also discussed by Dworzack [4] and by Verley.[6] A number of patents have appeared covering this reaction, in some of which a secondary alcohol such as isopropyl alcohol [7] is used in place of ethyl alcohol. Trichloroethyl alcohol is one of the chlorination products of alcohol and is found in the high-boiling fractions in the production of chloral.[8] It was prepared by Garzarolli-Thurnlackh [9] and by Delacre [10] by the action of diethylzinc on chloral.

[1] Ger. pat. 286,596 [Frdl. **12**, 29 (1914–16)].
[2] Houben, "Die Methoden der organischen Chemie," 3rd ed., Vol. 1, p. 595, Verlag Georg Thieme, Leipzig (1925).
[3] v. Bock, Dissertation, Albertus-Universität, Königsberg i. Pr. Germany (1926).
[4] Dworzack, Monatsh. **47**, 11 (1926).
[5] Meerwein and Schmidt, Ann. **444**, 233 (1925).
[6] Verley, Bull. soc. chim. [4] **37**, 537 (1925).
[7] Brit. pat. 235,584 [C. A. **20**, 917 (1926)]; Brit. pat. 286,797 [C. A. **23**, 395 (1929)]; U. S. pat. 1,725,054 [C. A. **23**, 4709 (1929)].
[8] Altschul and Meyer, Ber. **26**, 2758 (1893).
[9] Garzarolli-Thurnlackh, Ann. **210**, 63 (1881).
[10] Delacre, Bull. soc. chim. [2] **48**, 784 (1887).

XXX

VERATRONITRILE

(3,4-Dimethoxybenzonitrile)

$$(CH_3O)_2C_6H_3CHO + NH_2OH \rightarrow (CH_3O)_2C_6H_3CH{=}NOH + H_2O$$

$$(CH_3O)_2C_6H_3CH{=}NOH + (CH_3CO)_2O \rightarrow (CH_3O)_2C_6H_3CN + 2CH_3CO_2H$$

Submitted by J. S. Buck and W. S. Ide.
Checked by John R. Johnson and E. Amstutz.

1. Procedure

In a 1-l. round-bottomed flask, 83 g. (0.5 mole) of veratric aldehyde (Org. Syn. **13**, 102) is dissolved in 200 cc. of warm 95 per cent alcohol, and a warm solution of 42 g. (0.6 mole) of hydroxylamine hydrochloride (Org. Syn. Coll. Vol. 1, 311) in 50 cc. of water is added. The two solutions are mixed thoroughly and a solution of 30 g. (0.75 mole) of sodium hydroxide in 40 cc. of water is introduced. After the mixture has stood for two and one-half hours at room temperature, 250 g. of crushed ice is added and the solution is saturated with carbon dioxide. This causes the separation of the aldoxime as an oil which solidifies on standing overnight in an ice chest (Note 1). The crystalline oxime is filtered with suction, washed thoroughly with water, and allowed to dry in the air. The yield of oxime is 88–89 g. (97–98 per cent of the theoretical amount).

The veratraldoxime is placed with 100 g. of acetic anhydride (94–96 per cent) in a 300-cc. round-bottomed flask provided with a ground-glass air condenser (Note 2), and heated cautiously. A vigorous reaction takes place, and when this occurs the flame is removed. After the reaction has subsided the solution is refluxed gently for two hours and then poured carefully, with

stirring, into 300 cc. of cold water. The stirring is continued, and on cooling the nitrile separates in small, almost colorless crystals, which are filtered and dried in the air. The veratronitrile thus obtained is quite pure; it weighs 57–62 g. (70–76 per cent of the theoretical amount, based upon the veratric aldehyde), and melts at 66–67°.

2. Notes

1. Occasionally the oxime does not solidify after standing overnight. In this case it is advisable to separate the oily layer, treat with crushed ice, and induce crystallization by scratching. If a seed crystal of the oxime is available no difficulty is experienced.

2. If a cork or rubber stopper is used the product is likely to be colored.

3. Methods of Preparation

Veratronitrile has been obtained from 4-aminoveratrole by diazotization and treatment with cuprous cyanide[1] and by heating veratrylglyoxylic acid with hydroxylamine.[2] The general method employed above has been used for the preparation of a variety of substituted aromatic nitriles.[3]

[1] Moureu, Bull. soc. chim. [3] **15**, 650 (1896).
[2] Garelli, Gazz. chim. ital. **20**, 700 (1890) [Chem. Zentr. **62**, I, 61 (1891)].
[3] Marcus, Ber. **24**, 3656 (1891); Pschorr, Ann. **391**, 33 (1912).

APPENDIX

LATER REFERENCES TO PREPARATIONS IN THE PRECEDING VOLUMES

(The following references are to methods of possible preparative value that have recently been described. The numbers in parentheses following the name of the compound refer to the volume and page of Organic Syntheses.)

Adipic Acid (Coll. Vol. **1**, 18; **13**, 106, 110):

Use of catalysts and sulfuric acid to aid the oxidation of cyclohexanol by nitric acid. U. S. pat. 1,960,211 [C. A. **28**, 4435 (1934)].

***dl*-Alanine** (Coll. Vol. **1**, 20; **10**, 107):

From acetaldehyde and ammonium cyanide followed by hydrolysis. Fr. pat. 746,641 [C. A. **27**, 4541 (1933)].

Azelaic Acid (**13**, 4):

By the ozonation of oleic acid followed by oxidation. Ger. pat. 565,158 [C. A. **27**, 1008 (1933)].

Benzanthrone (**14**, 4):

By heating a mixture of anthraquinone, acetic anhydride, glycerol, and sulfuric acid to 150°. U. S. pat. 1,893,575 [C. A. **27**, 2163 (1933)]. From hydroquinone, glycerol, and sulfuric acid in the presence of a copper-iron or iron-zinc couple. Russ. pat. 29,475 [C. A. **27**, 4254 (1933)].

Benzoic Anhydride (Coll. Vol. **1**, 85):

From benzoyl chloride and benzoic acid at 220° under reduced pressure. U. S. pat. 1,948,342 [C. A. **28**, 2730 (1934)].

o-Bromophenol (**14**, 14):

Isolation from the products of the bromination of phenol at 170°. Rinkes, Rec. trav. chim. **30**, 77 (1911).

n-Butyl p-Toluenesulfonate (Coll. Vol. **1**, 139):

The yield is increased to 86 per cent using pyridine as the condensing agent. Sekera and Marvel, J. Am. Chem. Soc. **55**, 345 (1933).

Diphenylmercury (Coll. Vol. **1**, 223):

An 81 per cent yield is reported from phenylmagnesium bromide and mercuric bromide. Bachmann, J. Am. Chem. Soc. **55**, 2830 (1933).

Durene (**10**, 32; **11**, 101):

From crude xylene, formalin, and hydrogen chloride followed by reduction of the chloromethyl derivative with zinc dust and alkali. v. Braun and Nelles, Ber. **67**, 1094 (1934).

Ethyl Bromide (Coll. Vol. **1**, 27):

From ethylene and hydrogen bromide at −78° in the presence of anhydrous aluminum bromide. Tulleners, Tuyn, and Waterman, Rec. trav. chim. **53**, 549 (1934).

Ethylene Cyanohydrin (Coll. Vol. **1**, 251):

By mixing aqueous solutions of ethylene oxide and calcium cyanide at 10–20°. Ger. pat. 561, 397 [C. A. **27**, 998 (1933)].

Ethyl Oxomalonate (Coll. Vol. **1**, 261; **10**, 54, 110):

In 23–30 per cent yield by the oxidation of ethyl malonate with selenium dioxide. Astin, Newton, and Riley, J. Chem. Soc. **1933**, 391; Müller, Ber. **66**, 1668 (1933).

Fluorobenzene (**13**, 46):

It is recommended that the total hydrogen-ion concentration should not be greater than one mole per liter during the precipitation of the diazonium fluoborate. U. S. pat. 1,916,327 [C. A. **27**, 4539 (1933)].

Glycine (Coll. Vol. **1**, 292; **10**, 111; **13**, 107; **14**, 86):

From formaldehyde and ammonium cyanide followed by hydrolysis. Fr. pat. 746,641 [C. A. **27**, 4541 (1933)]. By the electrolytic reduction of cyanoformic esters. Ger. pat. 572,803 [C. A. **27**, 4180 (1933)].

Hydrogen Cyanide (anhydrous) (Coll. Vol. **1**, 307):

Ferrous sulfate facilitates the formation of hydrogen cyanide. The product is stabilized by the addition of two drops of concentrated hydrochloric acid per 500 g. of hydrogen cyanide and stored in an ice chest. Slotta, Ber. **67**, 1028 (1934).

Ketene (Coll. Vol. **1**, 324; **10**, 111; **13**, 107):

Preparation from acetone and method of purification to obtain a product stable at −80°. Rice, Greenberg, Waters, and Vollrath, J. Am. Chem. Soc. **56**, 1763 (1934).

3-Nitrophthalic Anhydride (Coll. Vol. **1**, 402):

A 44 per cent yield is reported from the direct nitration of phthalic anhydride. Hayashi and Kawasaki, J. Soc. Chem. Ind. Japan, **36**, 121 (1923) [C. A. **27**, 2947 (1933)].

Platinum Catalyst for Reductions (Coll. Vol. **1**, 452):

It is reported that a more active catalyst is obtained if potassium nitrate is used instead of sodium nitrate. Cook and Linstead, J. Chem. Soc. **1934**, 952.

Pyrrole (Coll. Vol. **1**, 461; **10**, 113):

By dry distillation of ammonium xylonate. Fang, Iowa State Col. J. Sci. **6**, 423 (1932) [C. A. **26**, 5919 (1932)].

Pyruvic Acid (Coll. Vol. **1**, 462; **10**, 114):

By the oxidation of methylglyoxal bisulfite. NEUBERG and KOBEL, Biochem. Z. **258**, 365 (1933).

Quinizarin (Coll. Vol. **1**, 464; **14**, 88):

From phthalic anhydride and diazotized *p*-chloroaniline. Brit. pat. 373,999 [C. A. **27**, 3946 (1933)]. From *p*-chlorophenol, phthalic anhydride, and aluminum chloride. U. S. pat. 1,886,237 [C. A. **27**, 1366 (1933)].

***dl*-Tartaric Acid** (Coll. Vol. **1**, 484):

By boiling *d*-tartaric acid for one week with dilute alkali. CAMPBELL, SLOTIN, and JOHNSTON, J. Am. Chem. Soc. **55**, 2604 (1933).

***p*-Tolualdehyde** (**12**, 80; **13**, 109):

Quantitative yields are reported from toluene, hydrogen cyanide, and hydrogen chloride in the presence of aluminum chloride at 100°. HENKEL, AYLING, and MORGAN, J. Chem. Soc. **1932**, 2793.

ADDITIONS AND CORRECTIONS FOR PRECEDING VOLUMES

(The numbers in parentheses following the name of the compound refer to the volume and page of Organic Syntheses. New methods or changes in procedure have not been checked unless otherwise noted.)

1-Amino-2-naphthol-4-sulfonic Acid (**11**, 12):

The gray product obtained by the method previously given is not quite pure and contains water of crystallization so that the percentage yield reported is in error. A better product can be obtained by stirring the mixture of nitroso-β-naphthol and sodium bisulfite solution vigorously by hand using a wooden paddle thus causing all of the soluble product to dissolve in three to four minutes. It is then filtered as rapidly as possible using two 15-cm. Büchner funnels and changing filter papers frequently. The clear, golden-yellow filtrate is acidified immediately on completion of the filtration. The product is then light gray, whereas if much time elapses before the bisulfite solution is acidified, the solution turns red and the aminonaphtholsulfonic acid may be deep purple-gray in color. After the product has been collected and washed with water, it is washed with warm alcohol until the filtrate is colorless, 1.5–2 l. being required. The product is washed with two 100-cc. portions of ether and dried to constant weight at 60–80° in the absence of light. A pure white, dust-dry product is thus obtained, weighing 370–380 g. (75–78 per cent of the theoretical amount based on the β-naphthol). The wash alcohol does not dissolve an appreciable amount of the aminonaphtholsulfonic acid since evaporation of the deep red wash liquor gives a dark residue weighing 3–4 g.

E. L. MARTIN and L. F. FIESER, private communication.

Benzanthrone (**14**, 4):

The quantity of sulfuric acid given in line 3 should be 1060 g. instead of 1060 cc.

C. F. H. ALLEN, private communication.

β-Benzoylpropionic Acid (**13**, 12):

The method previously described may be simplified and improved by adding 100 cc. of concentrated hydrochloric acid (sp. gr. 1.18) following the addition of water to the aluminum chloride complex, and removing the benzene by steam distillation. The hot mixture is transferred to a 1-l. beaker, and the β-benzoylpropionic acid separates as a colorless oil which soon solidifies. After cooling to 0°, it is collected, washed with a cold mixture of 50 cc. of concentrated hydrochloric acid and 150 cc. of water, and then with 200 cc. of cold water. The crude acid is dissolved in a solution of 75 g. of anhydrous sodium carbonate in 500 cc. of water by boiling for fifteen minutes. The solution is filtered by suction and the small amount of aluminum hydroxide washed twice with 50-cc. portions of hot water. Four grams of charcoal is added to the hot filtrate, the solution is stirred for three to four minutes and then filtered with suction. The clear, colorless filtrate is transferred to a 2-l. beaker, cooled to 50–60°, and carefully acidified with 130 cc. of concentrated hydrochloric acid. After cooling to 0° in an ice-salt bath the acid is filtered, washed well with water, dried overnight at room temperature and finally to constant weight at 40–50°. The yield is 110–115 g. (92–95 per cent of the theoretical amount). It melts at 114–115° and needs no further purification.

E. L. MARTIN and L. F. FIESER, private communication.

***d*- and *l*-Octanol-2** (Coll. Vol. **1**, 410):

The *sec.*-octyl hydrogen phthalate may be prepared in a purer state and with better yields if the reaction is carried out in the presence of pyridine according to the procedure used by LEVENE and MIKESKA, J. Biol. Chem. **75**, 594 (1927).

H. L. HALLER, private communication.

Pentamethylene Bromide (Coll. Vol. **1**, 419):

Pentamethylene bromide prepared by this method has been reported to contain a considerable amount of benzonitrile, and a procedure is given for removing it.

JOHNSON, J. Chem. Soc., **1933**, 1531.

Succinic Anhydride (**12**, 66):

A very convenient method of preparation is that of ANSCHÜTZ, Ann. **226**, 8 (1884). In a 1-l. round-bottomed flask fitted with a reflux condenser and a gas trap (Org. Syn. **14**, 2) are placed 118 g. (1 mole) of succinic acid and 215 cc. (235 g., 3 moles) of acetyl chloride, and the mixture is gently refluxed on the steam bath until the solid is all dissolved (1.5–2 hours). The solution is allowed to cool undisturbed and finally cooled in an ice bath. The anhydride, which separates in beautiful crystals, is collected on a Büchner funnel, washed with two 75-cc. portions of ether, and dried in a vacuum desiccator. The yield of material melting at 118–119° is 93–95 g. (93–95 per cent of the theoretical amount).

L. F. FIESER and E. L. MARTIN, private communication. Checked by C. R. NOLLER.

SUBJECT INDEX

(This Index Comprises Material from Volumes X to XV of this Series; for Previous Volumes see Collective Volume I.)

(Names in small capital letters refer to the titles of preparations which are given in full detail. A number in ordinary bold face type denotes the volume. A number in bold face italics refers to a page which gives preparative directions for a substance formed either as principal product or as a by-product, or to a product which has been prepared by a method analogous to the one given. Other numbers in ordinary type indicate pages on which a compound is mentioned incidentally or information is given concerning an item other than a compound.)

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